Less tachycardia during transnasal versus conventional gastroscopy

Anders U. Neuenschwander[1], Merete Christensen[1], Svend Schulze[1], Jacob Rosenberg[2] & Rete Trap[3]

INTRODUCTION: Transnasal endoscopy is well tolerated, but physiological benefits compared with conventional gastroscopy have not been studied in detail. The aims of this randomised study were to evaluate cardiopulmonary features, patient tolerance, and the endoscopist's evaluation of transnasal versus conventional endoscopy.

MATERIAL AND METHODS: Patients were randomized to either a conventionally sized transoral (50 patients) or to a transnasal endoscopy (48 patients). Pulse rate and oxygen saturation were registered as well as the patient's tolerance and the endoscopist's evaluation of the procedure.

RESULTS: The success rate for transnasal gastroscopy was 77%, mainly because of nasal stenosis. The per- and post-endoscopy pulse rates of the conventional group were elevated compared with those of the transnasal group ($p = 0.04$ and $p = 0.02$). Procedural discomfort in the two groups was similar, but significantly fewer transnasal patients reported gagging ($p < 0.01$). The endoscopists evaluated the technical features as good even if they did not reach those of conventional gastroscopy ($p < 0.05$).

CONCLUSION: In this study, transnasal gastroscopy was technically inferior to conventional gastroscopy. There was no benefit in terms of patient comfort, except for less gagging. A lower stress response was indicated by significantly lower pulse rates during transnasal than during conventional gastroscopy, but the clinical relevance of this finding needs to be further investigated.

FUNDING: not relevant.

TRIAL REGISTRATION: not relevant.

Oesophagogastroduodenoscopy is the gold standard investigation for upper gastrointestinal disorders. To make the procedure safer and more comfortable, thinner endoscopes for transnasal intubation have been designed [1-8]. Several trials have been conducted and they suggest that greater patient tolerance may be achieved by improving scope features, e.g. by minimizing its diameter [6, 9, 10]. This prospective, randomized study was conducted to evaluate the cardiopulmonary effects, patient tolerance, and the endoscopist's evaluation of the use of thin transnasal versus conventional transoral endoscopy.

MATERIAL AND METHODS

Outpatients referred to diagnostic upper gastrointestinal endoscopy were included consecutively after written informed consent had been obtained. The inclusion criteria were age over 18 years, Danish language proficiency, no history of disease in the nasal cavity and intended diagnostic endoscopy. A total of 98 patients were included and randomized to either conventional oral gastroscopy (OG) or transnasal gastroscopy (TG). The patients were randomized by consecutively numbered envelopes and a computer-generated code list.

The patients answered a questionnaire to clarify their previous experience with gastroscopy and their anxiety about the actual examination on a visual analogue scale (VAS) (VAS 0 = not anxious; 100 = could not be more anxious). A post-endoscopy questionnaire evaluated discomfort during the examination in general, during the introduction of the endoscope and during the rest of the examination (VAS; VAS 0 = no discomfort; 100 = discomfort could not be worse). The following parameters were assessed by answering yes or no: gagging; choking; pain from the nose, the throat and the stomach. The patients stated whether the degree of discomfort had been greater, lesser or as expected compared with their previous endoscopy experience, if any; whether they would prefer sedation in a future gastroscopy; and, finally, they stated their preference for a future procedure (OG or TG).

TG was performed using the Olympus GIF-N230 Videoscope (Olympus Optical Ltd., Tokyo, Japan) with an outer diameter of 6 mm (first 15 patients); and later the Olympus GIF-XP160 Videoscope (33 patients) with an outer diameter of 5.9 mm (**Figure 1**). OG was performed using the Olympus GIF-Q160 Videoscope with an outer diameter of 9.5 mm.

All patients received topical anaesthesia; before TG xylocain gel was inhaled into each nostril and before OG xylocain spray (10 mg/dose), four doses were spayed into the pharyngeal cavity. Intravenous sedation using midazolam was used only if specifically requested by the patient. The patients were positioned in the left lateral recumbent position during the procedures. The endoscopies were performed by experienced endoscopists.

Arterial oxygen saturation (SpO_2) and pulse rate (PR) were measured by a pulse oximeter (Nellcor Symphony N-3000, Nellcor Puritan Bennet Inc., Pleasanton, CA) twice at an interval of one minute be-

ORIGINAL ARTICLE

1) Department of Surgery, Glostrup Hospital
2) Department of Surgery, Herlev Hospital
3) Department of Surgery, Hospital of Southern Jutland

Dan Med J 2012;59(6):A4432

FIGURE 1

Transnasal endoscopy.

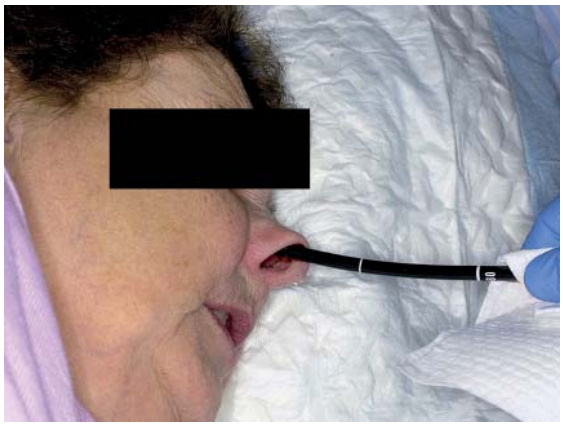
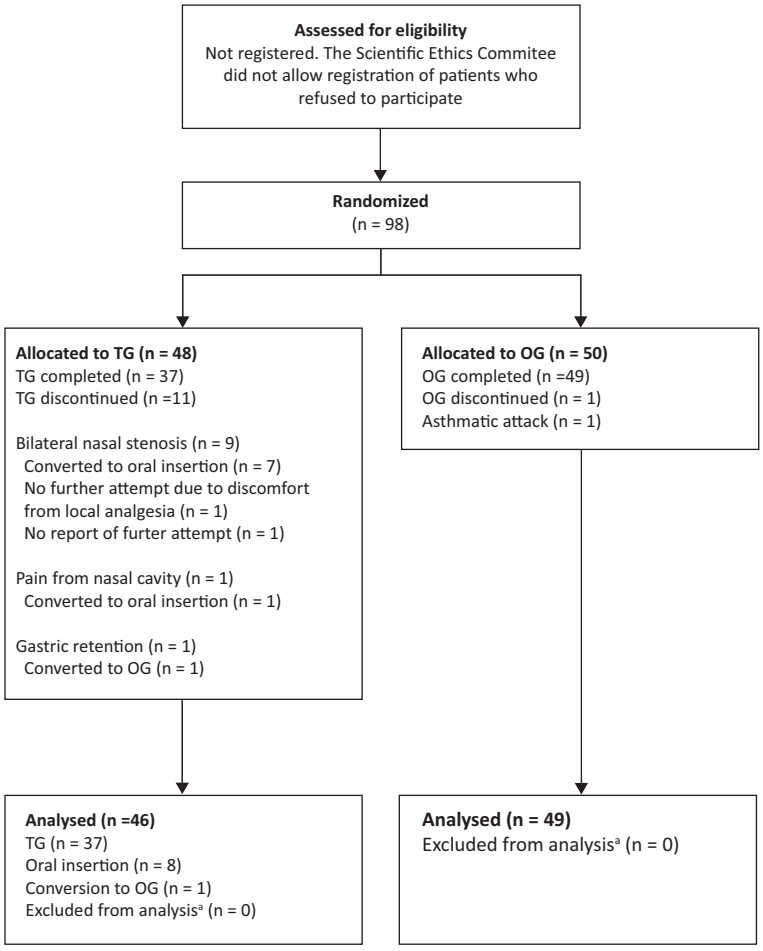


FIGURE 2

CONSORT diagram showing the flow of patients through the study [13].



OG = oral gastroscopy.
TG = transnasal gastroscopy.
a) Not all patients or all endoscopist's answered all questions.

fore the procedure; twice during the procedure (one and three minutes after intubation) and finally one and two minutes after extubation. The minimum SpO_2 and maximum PR were noted as was the duration of the procedure. Biopsies were taken when indicated, and the qualities were assessed by the pathologists. Adverse effects during the endoscopies were noted; e.g. epistaxis.

After the endoscopy, the endoscopists answered a questionnaire evaluating the following parameters using a VAS score: intubation (VAS 0 = not possible; 100 = very easy), ability to aspirate gastric contents (VAS 0 = not acceptable; 100 = perfect) and overview of the gastrointestinal tract (VAS 0 = not possible; 100 = perfect). The presence of chromatic aberrations and in case of TG, the presence of uni- or bilateral stenosis of the nasal cavity and looping in the oesophagus were also assessed. If TG could not be performed, the reasons were recorded. Finally, the endoscopists assessed their total subjective evaluation of the endoscopy on a one-to-six scale (one: unacceptable, six: perfect).

Statistics

Forty-one patients were needed in each group to achieve a statistical level of significance of 5% (type I error), a risk of type II error of 20% and a minimum relevant difference (MIREDIF) of 30% concerning our primary outcome parameter, which was tachycardia during the procedure. This was based on the 74% background incidence of tachycardia during gastroscopy [11]. For statistical analyses, we used non-parametric tests including Mann-Whitney, Wilcoxon, Friedman, Fisher's exact test and the χ^2 test as appropriate. Values are given as medians (ranges) if not otherwise stated. Differences were considered statistically significant when $p \leq 0.05$. A total of 48 patients were included into the TG group and 49 patients into the OG group (intention-to-treat group) and the results of these groups are stated in the text, figures and tables. All data were also evaluated with a per-protocol analysis and any differences from the intention-to-treat analysis are stated.

The protocol of this study was approved by the Copenhagen County Scientific Ethics Committee (KA 00066m). The study was initiated in 2000, i.e. before it became mandatory to register the trial in a public database [12].

Trial registration: not relevant.

RESULTS

The patient flow is shown in **Figure 2** [13]. Fifty patients were allocated to OG, but one procedure was interrupted due to an asthma attack. Thus, 49 patients were examined by OG, while 48 patients were allocated to TG. Eleven patients had their TG discontinued due to bi-

TABLE 1

General and cardiorespiratory results of the transnasal and transoral gastroscopy groups.

	Transnasal endoscopy (n = 46)	Oral endoscopy (n = 49)	p value
General data			
Age, median (range), years	56 (22-81)	58 (18-85)	ns
Gender, f/m, n	19/27	26/23	ns
Anxiety before endoscopy, median (range), VAS[a]	40.5 (0-100)	29.5 (0-100)	ns
Duration of endoscopy, median (range), min.	6.5 (3-14)	4.8 (2.5-26.5)	< 0.005
Biopsy,[b] n	8	12	ns
Sedation, n	3	4	ns
Pulse rate, median (range), beats/min.			
Before endoscopy	81 (60.5-118)	84,5 (54.5-113.5)	ns
During endoscopy	88.5 (63-127)	94 (67.5-151.5)	0.04
After endoscopy	83.25 (61.5-131)	91 (64-132.5)[c]	0.02
Tachycardia: pulse rate > 100 beats/min., n	23	31	ns
Maximum pulse rate during endoscopy, median (range), beats/min.	101 (68-143)	107 (68-154)	0.05
Saturation, median (range), SpO_2, %			
Before endoscopy	97.5 (94.5-100)	98 (92-100)	ns
During endoscopy	97.5 (93-100)	98 (88.5-100)	ns
After endoscopy	97.5 (84.5-100)	97.5 (90-100)	ns
Hypoxaemia: SpO_2 < 90%, n	1	4	ns

ns = non-significant. SpO_2 = arterial oxygen saturation. VAS = visual analogue scale value 0-100.
a) VAS score 100 = could not be more anxious; b) In three transnasal and four oral patients there was no report of the quality of the biopsy; c) After endoscopy the pulse rate for the transoral group was significantly elevated compared with the pre-procedural pulse rate ($p < 0.05$), which was not the case in the transnasal group.

lateral nasal stenosis (n = 9, seven women), pain in the nasal cavity or gastric retention. Thus, 37 patients were examined by TG, yielding a success rate of 77%. Demographic data, number of patients sedated and duration of examination are shown in **Table 1**. The nine patients converted from TG to transoral insertion of the thin endoscope (eight patients) or to conventional OG (one patient) were included in the TG group for the intention-to-treat analysis and in the OG group for the per-protocol analysis.

We found no difference between pre-endoscopic pulse rate levels between the groups (Mann Whitney, p = 0.6). There was a significant increase in pulse rate for both OG (84.5 versus 94 min-1) (Wilcoxon, p < 0.0001) and TG (81 versus 88.5 min-1) (Wilcoxon, p = 0.001) during endoscopy compared with the pre-endoscopy pulse rate (Table 1). Pulse rates during and after the endoscopy in the conventional group remained at a higher level than in the transnasal group (p = 0.04 and p = 0.02). The number of patients who had tachycardia (heart rate (HR) ≥ 100 min^{-1}) seemed to be higher during OG (n = 31 (65%)) than during TG (n= 23 (52%)), but the difference did not reach a level of statistical significance (χ^2, non-significant). However, the maximum pulse rate was higher during OG than during TG (107 versus 101 min^{-1}) (Mann Whitney, p = 0.05).

We found unchanged levels of oxygen saturation during both OG and TG (Friedmann, p = 0.68) (Table 1). Four patients developed hypoxaemia (SpO_2 < 90%) during OG (8.3%), one during TG (2.3%), p > 0.05. They were successfully treated with oxygen. None of the seven sedated patients developed hypoxaemia, but three patients developed tachycardia (HR ≥ 100 min^{-1}).

There was no significant difference between the levels of the reported overall discomfort between the two groups. However, the TG patients experienced less gagging than the OG patients (χ^2, $p < 0.01$) (**Table 2**). Pain from the throat and the stomach did not differ between the two groups, but more than half of the TG patients reported pain from the nose. Among the 21 TG patients who had previous experience with OG, 14 (67%) found the actual examination to be more comfortable. Only six of 19 OG patients (32%) with previous OG experience found the actual examination to be more comfortable. Wishes for sedation and endoscopy mode in a future gastroscopy are shown in Table 2.

More than 75% of the endoscopists experienced a perfect or almost perfect examination, although the overall performance of the transnasal endoscope and the ease of insertion was inferior to the conventionally sized endoscope and standard endoscopy (Mann Whitney, p = 0.003) (**Table 3**). There were four cases of accidental looping in the oesophagus, all among the first 15 TG patients. The overview of the mucosa was generally good, but not at par with that obtained with the conventional endoscope (Table 3). Only one TG case was characterized as completely unacceptable due to gastric retention. Significant chromatic aberrations were appar-

TABLE 2

Patient experiences with the present endoscopy and comparisons if possible with a previous endoscopy.

	Transnasal endoscopy			Oral endoscopy			
		n = 21			n = 19		
	n = 37[a]	+ sedation	– sedation	n = 49[b]	+ sedation	– sedation	p value
Score of discomfort, median (range), VASc							
The endoscopy in general	30 (0-100)			41 (0-100)			ns
Insertion of endoscope	47 (3-99)			37 (0-100)			ns
Rest of endoscopy	18 (0-100)			23 (0-100)			ns
Complaints, n/N (%)							
Gagging	12/37 (32)			35/49 (71)			< 0.01
Choking	3/36 (8)			12/49 (24)			ns
Pain from the neck	7/34 (21)			10/48 (21)			ns
Pain from the nose	20/36 (55)			–			–
Pain from stomach	6/36 (17)			3/44 (7)			ns
Wishes for future endoscopy, n							
Sedation (yes/no)	7/25			8/31			Not done
Transnasal (yes/no/indifferent)	20/3/14			4/7/31			Not done
Comparing with previous endoscopy the present endoscopy was, n							
Better		1	13		1	5	
The same		0	4		1	8	
Worse		0	3		0	4	

ns = non-significant. VAS = visual analogue scale value 0–100.
a) 37/46 patients had transnasal endoscopy performed; b) Not all patients answered; c) VAS score 100 = could not be more uncomfortable.

TABLE 3

Endoscopist's evaluation of scope features on a visual analogue scale (VAS), the values are median (range).

	Transnasal endoscopy (n = 44[a])	Oral endoscopy (n = 49)	p value
Insertion of endoscope, VAS[b]	83 (0-100)	98 (0-100)	0.003
Overview, VAS[b]			
Oesophagus	100 (20-100)	99 (85-100)	0.002
Stomach	97 (14-100)	99 (82-100)	0.001
Bulb	99 (22-100)	98.5 (77-100)	0.001
2nd portion	100 (13-100)	99 (85-100)	0.005
Suction ability, VAS[b]	81 (16-100)	99 (76-100)	< 0.0001

a) Only 44/46 endoscopies were evaluated by the endoscopist; b) VAS value 0-100. VAS score 100 = insertion: very easy, overview: perfect overview and suction: perfect effect of suction.

ent in six TG cases. Suction ability was better with the standard endoscope (Mann Whitney, $p < 0.0001$) (Table 3). The quality of biopsies during TG (n = 8) was sufficient for histopathologic evaluation.

During TG, eight cases of self-limiting epistaxis were observed, but no cases of haemorrhage required specialist therapy. One patient had severe gagging after TG, and two patients had discomfort from the pharyngeal anaesthesia before and after OG. Except for one mild asthmatic attack, there were no cardiopulmonary or other severe complications.

Per-protocol analysis

Because nine patients were converted from the transnasal group to the OG group (see Figure 2), it was necessary to re-analyse the results in the original setting. The per-protocol group then consisted of 58 patients in the OG group (49 + 9), while 37 patients remained in the TG group. The results (p values) for the two groups were similar for all issues eligible for comparison.

DISCUSSION

Although the transnasal method has been well evaluated [5-8], only few studies have evaluated cardiorespiratory parameters during transnasal endoscopy [14, 15].

We found indications of lower cardiac stress during the transnasal method, as the pulse rate did not reach the same high level as that of conventional endoscopy. This is in accordance with other controlled studies which have also showed fewer adverse effects on cardiopulmonary function in transnasal endoscopy than in the conventional oral procedure as evaluated by monitoring of pulse rate, blood pressure and oxygen saturation [14, 15]. Tachycardia as well as a classic stress response has been described at conventional endoscopy [11, 16-19]. The significance of tachycardia or raised rate-pressure product (pulse rate × systolic blood pressure) is not fully known; however, it may be associated with previous findings of ST segment changes documented by Holter monitoring during endoscopy [11, 16, 20], which could

not be resolved by administration of oxygen [11]. Myocardial scintigraphies have shown reduced myocardial blood flow during endoscopic retrograde cholangiopancreatography [17], but it remains unclear whether there is any clinical relevance of e.g. a difference in maximum pulse rate of six beats per minute between TG and OG.

The oxygenation of patients has been reported both to increase and to decrease during transnasal endoscopy independently of the diameter of the endoscope [1, 4]. Our findings are in accordance with the findings of Banks et al [1] who concluded that the level of saturation dropped with longer intubation time and with prolonged examination of the pharyngeal area.

Reported success rates for transnasal endoscopy range from 76% to 100%, the main cause of failure being nasal stenosis [2-8, 10]. Thus, our success rate of 77% was in the lower end, but the majority of failures were due to patients with nasal stenosis.

Previous assessments of the technical features of the two methods are in accordance with the present study by documenting that TG was more time-consuming [7, 8], has a lower success rate and is often associated with a lower technical quality than transoral endoscopy. Other studies however, found no significant difference in duration [5, 6], and Garcia et al 2003 [9] found that the duration of unsedated TG was shorter than that of sedated OG. The present study showed less overview of the stomach; and though the difference between the VAS scores seems very small, this was also found by others [7].

Some of the difference between the more standardized OG method and TG is explained by familiarity with the conventional endoscope and the route of insertion. It is quite obvious that a learning curve is linked to the TG procedure, which is also illustrated in the present study, where looping of the transnasal endoscope happened only in the first part of the study.

In our study, patients undergoing TG experienced significantly less gagging. This has also been documented in some other studies [6], but not in all [7]. This study documented that patients with previous OG experience tolerated TG better than OG. This is in line with a study which found that 91% of patients with previous OG experience would prefer TG in a future gastroscopy [3]. More patients undergoing TG than OG wished the "same again". This is a confirmation of previous findings comparing TG and OG [6, 7].

Oral insertion of the thin endoscope seems to be a way of diminishing pain during insertion [6-8], but the problems of gagging and choking appear to be comparable to those seen in conventional oral endoscopy [6, 7, 9]. Moreover, transnasal endoscopy is feasible with the patient sitting in a chair and being able to communicate during the procedure [10].

Serious complications of TG are rare; however, a previous study reported a single case of high oesophageal perforation [8]. We found 22% with mild epistaxis; this is similar to the frequency (2 to 22%) found in the literature [3, 5-7].

CONCLUSION

In our hands, TG using a thin endoscope with a diameter of six millimetres was more time-consuming than and technically inferior to conventional OG. Patients reported significantly less gagging, but we found no benefit in overall patient comfort. The major obstacles seemed to be pain from the nose and nasal stenosis generating a high conversion rate from nasal to oral intubation. Other endoscopists, however, have found negligible conversion rates, and the method may therefore be feasible in other hands. Interestingly, we found a lower stress response indicated by significantly lower pulse rates during TG, but the clinical relevance of this finding needs to be further investigated.

CORRESPONDENCE: *Anders U. Neuenschwander,* Kirurgisk Afdeling, Hillerød Hospital, 3400 Hillerød, Denmark. E-mail: aun@hih.regionh.dk

ACCEPTED: 2 March 2012

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk
A complete list of references can be obtained from the authors.

LITERATURE

1. Banks MR, Kumar PJ, Mulcahy HE. Pulse oximetry saturation levels during routine unsedated diagnostic upper gastrointestinal endoscopy. Scand J Gastroenterol 2001;36:105-9.
2. Faulx AL, Catanzaro A, Zyzanski S et al. Patient tolerance and acceptance of unsedated ultrathin esophagoscopy. Gastrointest Endosc 2002;55:620-3.
3. Dumortier J, Napoleon B, Hedelius F et al. Unsedated transnasal EGD in daily practice: results with 1100 unsedated consecutive patients. Gastrointest Endosc 2003;57:198-204.
4. Christensen M, Achiam M, Trap R et al. Transnasal gastroscopy. Dan Med Bull 2000;41:218-20.
5. Craig A, Hanlon J, Dent J et al. A comparison of transnasal and transoral endoscopy with small diameter endoscopes in unsedated patients. Gastrointest Endosc 1999;49:292-6.
6. Preiss C, Charton JP, Schumacher B et al. A randomized trial of unsedated transnasal small-caliber esophagogastroduodenoscopy (EGD) versus peroral small-caliber EGD versus conventional EGD. Endoscopy 2003; 35:641-6.
7. Birkner B, Fritz N, Schatke W et al. A prospective randomized comparison of unsedated ultrathin versus standard esophagogastroduodenoscopy in routine outpatient gastroenterology practice: Does it work better through the nose? Endoscopy 2003;35:647-51.
8. Zaman A, Hahn M, Hapke R et al. A randomized trial of peroral versus transnasal unsedated endoscopy using an ultrathin videoendoscope. Gastrointest Endosc 1999;49:279-84.
9. Garcia RT, Cello JP, Ngyen MH et al. Unsedated ultrathin EGD is well accepted when compared with conventional sedated EGD: a multicenter randomized trial. Gastroenterology 2003;125:1606-12.
10. Dean R, Dua K, Massey B et al. A comparative study of unsedated transnasal esophagogastroduodenoscopy and conventional EGD. Gastrointest Endosc 1996;44:422-4.
11. Rosenberg J, Stausholm K, Andersen IB et al. No effect of oxygen therapy on myocardial ischemia during gastroscopy. Scand J Gastroenterol 1996;31:200-5.
12. De Angelis C, Drazen JM, Frizelle FA et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. Ann Intern Med 2004;141:477-8.
13. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Med 2010;7:e1000251.
14. Yuki M, Amano Y, Komazawa Y et al. Unsedated transnasal small-caliber esophagogastroduodenoscopy in elderly and bedridden patients. World J Gastroenterol 2009;15:5586-91.
15. Yagi J, Adachi K, Arima N et al. A prospective randomized comparative

study on the safety and tolerability of transnasal esophagogastroduodenoscopy. Endoscopy 2005;37:1226-31.
16. Yazawa K, Adachi W, Koide N et al. Changes in cardiopulmonary parameters during upper gastrointestinal endoscopy in patients with heart disease: Towards safer endoscopy. Endoscopy 2000;32:287-93.
17. Christensen M, Hendel HW, Rasmussen V et al. Endoscopic retrograde cholangiopancreatography causes reduced myocardial blood flow. Endoscopy 2002;34:707-800.
18. Tønnesen H, Puggaard L, Braagaard J et al. Stress response to endoscopy. Scand J Gastroenterol 1999;34:629-31.
19. Oei-Lim VLB, Kalkman CJ, Bartelsman JFWM et al. Cardiovascular responses, arterial oxygen saturation and plasma catecholamine concentration during upper gastrointestinal endoscopy using conscious sedation with midazolam or propofol. Eur J Anaesthesiol 1998;15:535-48.
20. Johnston SD, McKenna A, Tham TCK. Silent myocardial ischemia during endoscopic retrograde cholangiopancreatography. Endoscopy 2003;35: 1039-42.