Results report for clinicaltrialsregister.eu

The study has not yet been published in a medical journal

This was a randomized, triple-blind, non-inferiority trial conducted at the Digestive Disease Center, Bispebjerg Hospital. Participants were recruited from patients scheduled for elective esophagogastroduodenoscopy (gastroscopy) in the Endoscopy Unit and were randomly assigned to receive either viscous lidocaine or placebo prior to the procedure. The trial was prospectively registered on ClinicalTrials.gov (NCT04725695) before the start of recruitment.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Danish Medicines Agency (EudraCT number 2020-005177-27) and the Danish Research Ethics Committee (H-21021416). It was monitored by the Danish Good Clinical Practice Unit.

Participants

Eligible participants were adults aged 18 to 75 years scheduled for elective, outpatient gastroscopy. Exclusion criteria included: known cognitive impairment, dysphagia, allergy to lidocaine, suspected gastric retention, insufficient proficiency in the Danish language, or a planned procedure involving nurse-assisted propofol sedation.

All participants were given at least 24 hours to consider participation and provided both oral and written informed consent. Intraprocedural data were documented by one of two dedicated endoscopy nurses. Post-procedure assessments were completed by the endoscopist immediately after the procedure. All study data were entered into a secure electronic database (REDCap) by project staff.

Intervention

Participants were randomly assigned to receive 5 mL of either viscous lidocaine (20 mg/mL) or placebo, administered orally prior to the procedure. Both preparations were compounded by the Capital Region of Denmark Pharmacy to have similar viscosity, color, and licorice flavor to ensure blinding.

Participants, clinical staff (including endoscopists and nurses), and the data analyst were blinded to the allocation. Intravenous midazolam and/or alfentanil were offered according to routine clinical indications at the discretion of the treating team.

Outcomes

The primary outcome was the endoscopist's assessment of the ease of esophageal intubation, rated on a numeric rating scale (NRS) from 0 ("very easy") to 10 ("very hard"). Secondary outcomes included:

1. Endoscopist's rating of the overall procedure ease (same NRS as above)
2. Patient-reported procedural discomfort on a NRS from 0 ("no discomfort") to 10 ("worst imaginable discomfort")
3. Patient reported willingness to repeat the procedure under the same conditions on a NRS from 0 ("not willing") to 10 ("willing")
4. Number of attempts to intubate the esophagus
5. Number of times the gag reflex was activated
6. Use of intravenous sedation (yes/no), and
7. Total doses of midazolam and alfentanil administered.

Additionally, both the endoscopist and the assisting nurse were asked to predict the participant's treatment allocation (viscous lidocaine or placebo).

Randomization and Blinding

Randomization was performed using a concealed sequence, ensuring allocation concealment and maintaining triple blinding (participants, clinical staff, and data analysts).

Statistical Analysis

The hypothesis was that placebo would be non-inferior to viscous lidocaine for the primary outcome. Sample size was calculated to detect a non-inferiority margin of 1 point on the NRS, assuming a standard deviation of 3, with 80% power and a two-sided significance level of 5%, allowing for a 10% dropout rate. This required a total of 124 participants per group.

The primary outcome was non-normally distributed, and the median difference between groups with 95% confidence intervals was calculated using the bootstrap method with percentile intervals. Other continuous and ordinal outcomes were also non-normally distributed and analyzed using the Wilcoxon rank-sum test. Dichotomous outcomes were analyzed using the χ^2 test.

Predictive accuracy for treatment allocation was reported as sensitivity, specificity, and area under the curve (AUC). All analyses were performed using R version 3.6.1 (The R Foundation for Statistical Computing) with the packages boot, ggplot2, Publish, and pROC.

Results

In total, 119 patients were randomized to receive either placebo or viscous lidocaine. Of these, 114 participants were included in the analyses (Fig. 1). Five participants were excluded because they did not undergo gastroscopy, all for reasons unrelated to the allocated treatment. Recruitment took place between March 23, 2022, and September 22, 2023. The study was paused in October 2023 and was ultimately terminated on October 21, 2024, due to limited research staff resources. Baseline characteristics of the analyzed patients are presented in Table 1.

The endoscopist's assessment of esophageal intubation ease yielded a median score of 2 (interquartile range 1–3) in both the viscous lidocaine and placebo groups (Fig. 2). The median difference was 0, with a 95% confidence interval of –1 to 1 (Fig. 3). There were no statistically significant differences between groups in any of the secondary outcomes (Table 2).

The accuracy of treatment allocation prediction by the endoscopist and the assisting endoscopy nurse showed a sensitivity of 44.3% and 49.2%, a specificity of 56.4% and 61.8%, and AUC of 0.504 and 0.548, respectively.

No adverse events or adverse reactions were reported.

Fig 1.

CONSORT Flow Diagram

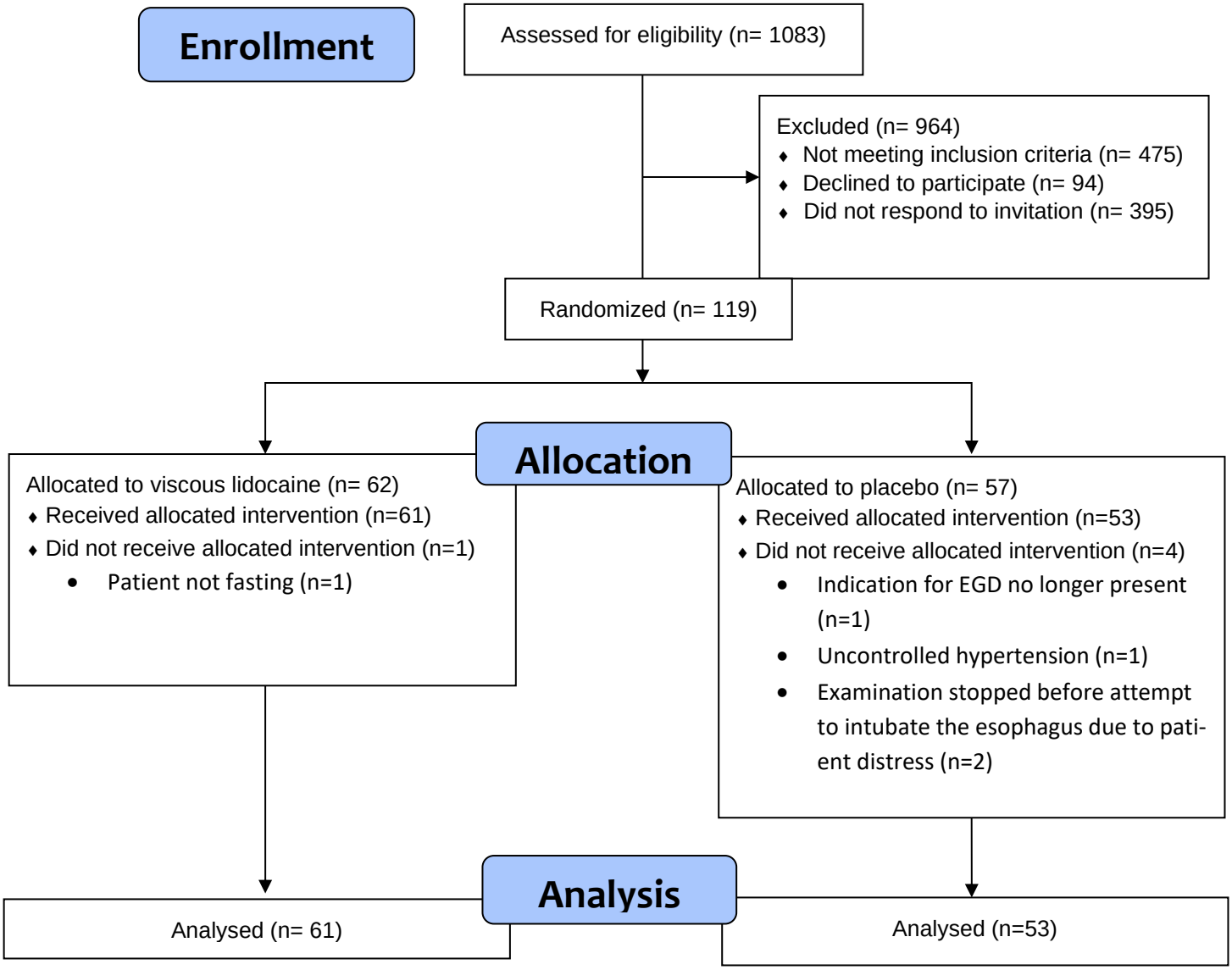

Fig 2.

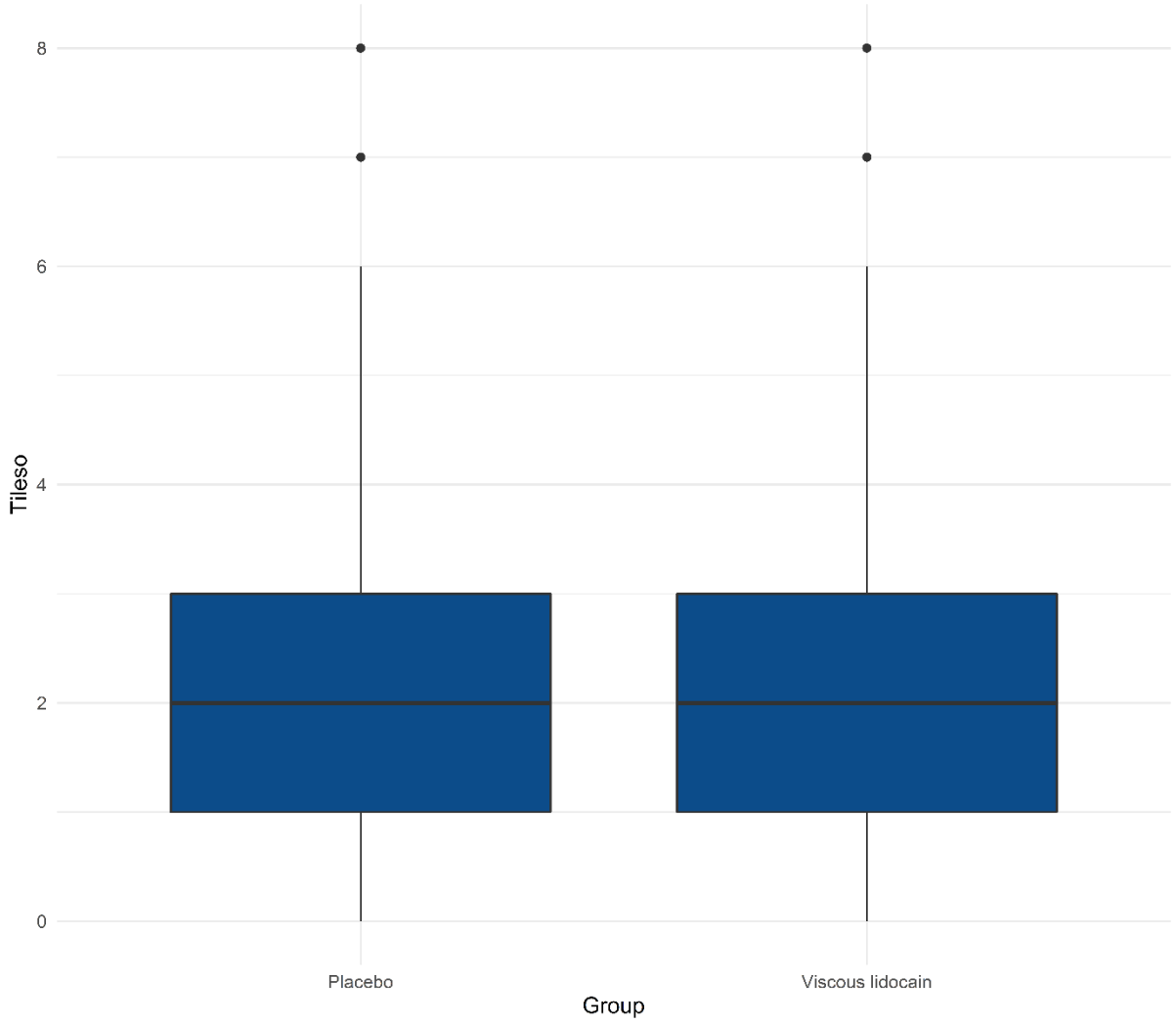

Figure 3. Median difference in the endoscopist's assessment of the ease of esophageal intubation on a numeric rating scale from 0 to 10

Fig 3

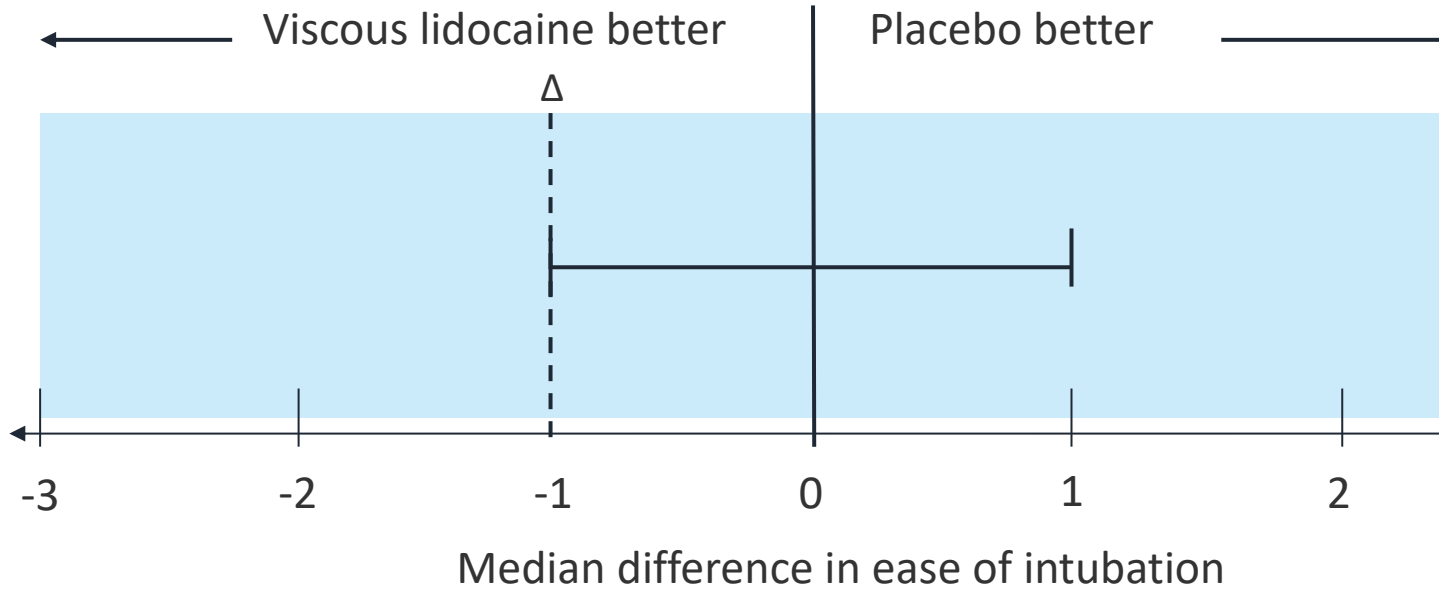

Figure legend: Error bars indicate 95% confidence interval. Dashed line marked Δ at x = 1 indicates the noninferiority margin.

Table 1. Characteristics of patients included for analysis

Characteristics	Viscous lidocain N = 61	Placebo N = 53	Total N = 114
Female gender	30 (49.2)	28 (52.8)	58 (50.9)
Age, years			
18-32	7 (11.5)	4 (7.5)	11 (9.6)
33-47	8 (13.1)	6 (11.3)	14 (12.3)
48-62	16 (26.2)	14 (26.4)	30 (26.3)
63-75	30 (49.2)	29 (54.7)	59 (51.8)
		75.2	77.1
Weight, kg	78.8 (17.3)	(20.0)	(18.6)
BMI, kg/m2	26.1 (5.6)	25.1 (5.5)	25.7 (5.5)
Pre-examination self-percieved pharyngeal reflex			
Strong	17 (27.9)	20 (37.7)	37 (32.5)
Normal	42 (68.9)	31 (58.5)	73 (64.0)
Weak	2 (3.3)	2 (3.8)	4 (3.5)
History of previous EGD	37 (60.7)	38 (71.7)	75 (65.8)
Indication for the EGD			
Anemia	9 (14.8)	4 (7.5)	13 (11.4)
Assessment of esophageal varices	1 (1.6)	0 (0.0)	1 (0.9)
Control	20 (32.8)	16 (30.2)	36 (31.6)
Abdominal pain	3 (4.9)	6 (11.3)	9 (7.9)
Reflux symptoms	4 (6.6)	6 (11.3)	10 (8.8)
Other	24 (39.3)	21 (39.6)	45 (39.5)
Endoscopist's prior EGD count			
>100	54 (88.5)	48 (90.6)	102 (89.5)
50-100	6 (9.8)	5 (9.4)	11 (9.6)
0-50	1 (1.6)	0 (0.0)	1 (0.9)

The values given are N (%) or mean (SD). BMI, body mass index; EGD, esophagogastroduo-denoscopy

Table 2. Secondary outcomes

	Viscous lidocain	Placebo	Total	
Outcome	**N = 61**	**N = 53**	**N = 114**	**P**
Attempts to reach the esophagus	1 (1-1)	1 (1-1)	1 (1-1)	0.916
Full examination score, NRS 0-10	2 (1-3)	2 (1-3)	2 (1-3)	0.821
Recieved intravenous sedation	48 (78.7)	44 (83.0)	92 (80.7)	0.729
Midazolam, mg	2.0 (1.0-2.0)	2.0 (2.0-3.0)	2.0 (1.3-3.0)	0.877
Alfentanil, mcg	0.0 (0.0-0.0)	0 (0.0-0.5)	0.0 (0.0-0.0)	0.186
Discomfort score, NRS 0-10	5 (3-7)	6 (3-7)	5 (3-7)	0.444
Willingness score, NRS 0-10	10 (10-10)	10 (10-10)	10 (10-10)	0.839
Number of gag reflex activations	12 (7-20)	16 (7-23)	14 (7-22)	0.309

Numbers are median (interquartile range) or N (%)