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The effect of a mesenteric traction syndrome on internal carotid artery blood flow

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Purpose: During abdominal surgery, manipulation of internal organs may induce a "mesenteric traction syndrome" (MTS) including a triad of flushing, hypotension, and tachycardia that lasts for approximately 30 min. We evaluated whether MTS affects internal carotid artery blood flow.

Methods: This prospective cohort study included 27 patients aged 65 ± 11 years (mean ± SD) undergoing stomach resection (n = 12), esophageal resection (n = 14), or gastro-entero anastomosis (n = 1) during propofol-remifentanil and thoracic epidural anesthesia. Duplex ultrasound determined internal carotid artery blood flow, laser Doppler flowmetry assessed forehead skin blood flow, and near-infrared spectroscopy determined cerebral oxygenation. Development of MTS was defined by flushing within 60 min after incision.

Results: Seven patients developed MTS 22 [20–26; median (IQR)] min after incision and at that time the change in heart rate (to 87 ± 13 vs. 70 ± 11 bpm; $P = 0.0007$) and skin blood flow (to 214 (134–269) vs. 84 (59-112 PU; $P = 0.0044$) was higher in the patients who developed MTS as compared to those who did not, while mean arterial pressure (63 ± 13 vs. 64 ± 14 mmHg; $P = 0.1433$), cerebral oxygenation (69 ± 9% vs. 63 ± 10%; $P = 0.2485$), and internal carotid artery flow (225 ± 53 vs. 203 ± 69 ml/min; $P = 0.9529$) were similar.

Conclusion: Hemodynamic perturbations are observed in some patients in response to manipulation of the viscera, but the development of MTS appears not to influence internal carotid artery flow.

Clinical trial registration: https://clinicaltrials.gov/ct2/show/NCT02951273?term=NCT02951273&rank=1, identifier: NCT02951273.

KEYWORDS

anesthesia, internal carotid artery, cerebrovascular circulation, near-infrared spectroscopy, skin blood flow, surgery, mesenteric traction syndrome, cerebral blood flow

1. Introduction

Traction of the viscera during abdominal surgery may provoke a so-called mesenteric traction syndrome (MTS) described as a triad of flushing, tachycardia, and hypotension [1–4]. MTS is part of the inflammatory response to surgery [5] and with marked flushing, MTS associates with postoperative complications [1]. The incidence of MTS is reported in approximately 50% of patients undergoing open upper gastrointestinal, pancreatic, and abdominal aortic surgery [1–4, 6] and develops about 15–20 min after incision and lasts for some 30 min [4, 6]. The syndrome is characterized by vasodilation with an increase in cardiac output [3, 4] but the effect of MTS on cerebral blood flow (CBF) is unclear.

Development of MTS is reported to elevate near-infrared-spectroscopy determined cerebral oxygenation S_cO_2 [4], which may relate to an increase in CBF or be due to an increase in forehead skin blood flow (SkBF) as changes in the extracranial circulation influence S_cO_2 [7]. Furthermore, MTS appears not to affect transcranial Doppler-determined middle cerebral artery blood velocity [4], but the evaluation is limited in response to vasodilation that may affect the diameter of the middle cerebral artery whereby any increase in blood flow is underestimated [8]. MTS likely relates to the release of prostaglandin I_2 (PGI_2) as MTS is absent following cyclooxygenase inhibition [2, 3, 9]. Infusion of PGI_2 to healthy subjects provokes similar hemodynamic changes as MTS with no effect on CBF [10], although PGI_2 dilates cerebral vessels *in vitro* [11, 12]. Furthermore, the effect of PGI_2 on CBF could be influenced by anesthesia and other vasodilators potentially released during MTS. Thus, we designed the study to evaluate whether CBF is elevated in response to MTS or whether the increase in S_cO_2 is due to the increase in SkBF. An increase in CBF in response to MTS could be clinically important as it may elevate intracranial pressure and provoke cerebral edema [13–15].

This study evaluated whether the development of MTS in patients undergoing stomach or esophageal resection affects internal carotid artery (ICA) blood flow and we hypothesized that ICA flow, SkBF, and S_cO_2 would increase in response to MTS. Duplex ultrasound was used to evaluate ICA flow which correlates to an evaluation by phase contrast magnetic resonance imaging [16].

2. Materials and methods

2.1. Participants

A total of 30 consecutive patients planned for open stomach- or esophageal resection aged 18 years or older were included in this prospective cohort study (from December 2016 to July 2017) and provided written informed consent as approved by the ethical committee of Copenhagen (H-16036250, 18 October 2016) in accordance with the Declaration of Helsinki. The study was preregistered on ClinicalTrials.gov (NCT02951273; principal investigator: N.D.O.; 1 November 2016) and the manuscript adheres to the STROBE guideline. Results from this study concerning the effect of induction of anesthesia, phenylephrine treatment of anesthesia-induced hypotension, and cerebral CO_2 reactivity is published elsewhere [17]. Exclusion criteria were intake of anti-inflammatory medication including non-steroidal anti-inflammatory drugs and corticosteroids, robot-assisted procedure, >15% ICA obstruction as evaluated by duplex ultrasound 1 to 3 days prior to surgery, and neurologic disease that may affect CBF including stroke, dementia, and epilepsy. Any use of acetylsalicylic acid was discontinued for 3 days prior to surgery and no anti-inflammatory medication was used during anesthesia.

2.2. Surgical setting

Surgery was after an overnight fast with patients allowed to drink "clear" fluids until 2 h before the scheduled time for the operation and no premedication was administered. Under the cover of local anesthesia, a radial artery and epidural catheter (T8–T10) was placed. Epidural anesthesia was by 15–30 mg bupivacaine, followed by infusion of bupivacaine with morphine (2.5 and 0.05 mg/ml; 5 ml/h) and an hourly bolus dose administration of 15 mg bupivacaine. Anesthesia was induced by propofol and maintained by propofol and remifentanil. Muscle relaxation was by cisatracurium or suxamethonium allowing for tracheal intubation and ventilation aimed at an end-tidal CO_2 tension of 4.0–5.0 kPa (Dräger Primus, Drägerwerk, Lübeck, Germany). A central venous catheter was inserted in the internal jugular vein contralateral to the ICA insonation site. Blood volume was maintained by human albumin 5% and lactated Ringer's solution. A reduction in mean arterial pressure (MAP) to below 60 mmHg was treated by administration of a bolus dose of ephedrine or phenylephrine or infusion of noradrenaline on the choice of the anesthesiologist.

2.3. Definition of a mesenteric traction syndrome

Development of MTS was defined as flushing within 60 min after incision in patients who underwent manipulation of the abdominal viscera. Flushing was described as level "I" if around the eyes and on the cheeks and level "II" if it covered the entire face [1, 2, 4, 6].

2.4. Measurements

Radial artery catheterization allowed for the evaluation of blood gas variables (ABL 725, Radiometer, Copenhagen, Denmark) as well as MAP, heart rate (HR), stroke volume (SV), cardiac output (CO), and total peripheral resistance (TPR; Finometer, Finapres Medical Systems, Amsterdam, The Netherlands). Duplex ultrasound determined ICA flow using a linear transducer at 8–12 MHz (Logiq E, transducer 12L, GE Medical System, Jiangsu, China). The evaluation was ≥1.5 cm distal to the bifurcation with the head rotated to the contralateral side. At an insonation angle ≤60° pulsed-wave Doppler determined the angle-corrected time-averaged maximum blood velocity that corresponds to two times the mean velocity [18]. Software determined diameter (Brachial Analyzer for Research v. 6, Medical Imaging Applications LLC, Coralville, IA, USA) and two to three recordings over approximately 20 s were conducted, and the mean reported with flow calculated as follows [19]:

$$\text{ICA flow} = \pi * (\text{diameter}/2)^2 * (\text{Time averaged maximum blood velocity})/2$$

Conductance was ICA flow divided by MAP.

The S_cO_2 was determined on the forehead ipsilateral to the evaluation of ICA flow and right deltoid muscle oxygenation (INVOS 5100C, Somanetics, Troy, MI, USA) using an optode with a 3 and 4 cm emitter-receiver separation and wavelengths of 730 and 808 nm. The arterial CO_2 tension ($PaCO_2$) influences CBF [20], and thus, ICA flow and S_cO_2 are reported after correction for any changes in $PaCO_2$ from before induction of anesthesia using the individual CO_2 reactivity as determined in the present study (CO_2 reactivity for the ICA: 18 [14–24]%/kPa and S_cO_2: 3.6 (3.1–4.5)%/kPa, respectively,

as published elsewhere [17]) and the corrected flow was calculated as follows:

$$\text{Corrected ICA flow} = \text{measured ICA flow} * (1 - \text{CO}_2 \text{ reactivity} * \text{change in PaCO}_2)$$

The same formula was used for S_cO_2.

Laser Doppler flowmetry with an integrated oxygenation sensor evaluated forehead SkBF, oxy- and deoxyhemoglobin concentration (O_2HB_{skin} and HB_{skin}), and thus skin oxygenation [$O_2HB_{skin}/(O_2HB_{skin} + HB_{skin})$] close to the hairline at a depth of 1–2 mm (VMS-LDF and VMS-OXY, Moor Instruments, Axminster, UK). The depth of anesthesia was assessed by the bispectral index (BIS Complete Monitoring Systems, Covidien, USA). Arterial gas variables and ICA flow were evaluated 5 min before and after incision and 0, 20, 40, and 70 min after flushing and correspondingly after 20, 40, 60, and 90 min after incision in patients who did not develop MTS.

Central hemodynamic and skin variables were sampled at 100 Hz (Powerlab, ADInstruments, Bella Vista, Australia) and S_cO_2, muscle oxygenation, and bispectral index every 5 s on a pc, and values were averaged over 2 min. Volume balance and vasopressor administration from 0 to 90 min after the incision was recorded from the anesthesia chart. All measurements were conducted prior to one-lung ventilation for patients undergoing esophageal resection.

TABLE 1 Patient characteristics.

	Patients with MTS ($n = 7$)	Patients without MTS ($n = 20$)	*P*-value
Age (years)	64 ± 9	66 ± 12	0.7025
Height (cm)	178 ± 3	169 ± 8	0.0085
Weight (kg)	96 ± 16	72 ± 15	0.0014
Body mass index (kg m^{-2})	30 ± 5	25 ± 4	0.0171
Male, *n* (%)	6 (86%)	8 (40%)	0.0768
Preoperative risk factors			
ASA physical status II, *n* (%)	6 (86%)	11 (55%)	0.204
ASA physical status III, *n* (%)	1 (14%)	9 (45%)	0.204
Arterial hypertension, *n* (%)	3 (43%)	10 (50%)	1
Dyslipidemia, *n* (%)	0 (0%)	6 (30%)	0.1548
Diabetes mellitus type 2, *n* (%)	1 (14%)	2 (10%)	1
Chronic obstructive pulmonary disease, *n* (%)	0 (0%)	3 (15%)	0.5453
Chronic heart failure NYHA II, *n* (%)	0 (0%)	2 (10%)	1

Values are mean ± SD or count. ASA, American Society of Anesthesiologists physical status classification; NYHA, New York Heart Association classification.

2.5. Statistical analysis

2.5.1. Sample size calculation

Reperfusion of a grafted liver during orthotopic liver transplantation is followed by a hemodynamic response similar to that manifesting with the development of MTS and is accompanied by an approximately a 23% increase in CBF when taking into account the concomitant increase in $PaCO_2$ [21] and a sample size calculation indicated that at least six patients who developed MTS were required to detect a similar increase in ICA flow with an SD for the change of 15% [22] at a 5% significance level and a power of 80%.

2.5.2. Outcome

The primary outcome was a change in ICA flow while secondary outcomes were change in S_cO_2, SkBF, and skin oxygenation from before incision to the start of flushing in patients who developed MTS as compared to those who did not (i.e., the interaction of time point and group according to development of MTS, see below).

2.5.3. Statistics

An analysis of variables was performed by a repeated measures mixed model, fit by restricted maximum likelihood in a structured covariance model with fixed effects, (1) time point (Time; 5 min before and after incision and 0, 20, 40, and 70 min after flushing and correspondingly 20, 40, 60, and 90 min after incision in patients without MTS), (2) group according to development of MTS, and (3) the interaction of time point and group, and the subject variable as a random effect (Proc mixed; SAS 9.4, SAS Institute, Cary, NC, USA). The interaction factor was evaluated at the five time points following baseline in order to evaluate whether changes from baseline were different in the patients who developed MTS as compared to those who did not and the Bonferroni method was used to correct for multiple testing ($P < 0.01$ for the interaction factor). If the factor "time point" was significant, we evaluated changes from baseline for both groups combined using the mixed model with correction for multiple comparisons by the Tukey-Kramer method. In case the interaction factor was significant, changes over time were evaluated for patients with and without MTS separately using a repeated measures mixed model with the fixed effect time point and the subject variable as a random effect in order to evaluate changes from baseline with correction for multiple comparisons by the Tukey-Kramer method. Analysis of SkBF, O_2HB_{skin}, HB_{skin}, plasma lactate, the fraction of inspired O_2, and infusion of propofol and remifentanil were conducted after logarithmic transformation. Differences in age, height, weight, and body mass index among patients with and without MTS were evaluated by unpaired *t*-test. Differences between the groups regarding volume balance and vasopressor administration from 0 to 90 min after the incision was evaluated by Wilcoxon-Mann-Whitney's test. Furthermore, differences in preoperative risk factors, gender, and length of stay were evaluated by Fisher's exact test. The figure was drawn in SigmaPlot 14.0 (Systat Software Inc., CA, USA). Values are presented as mean ± SD or median (IQR) for not normally distributed data, estimates by mixed models for the interaction factor upon flushing are mean (95% CI), and changes are reported as absolute values. Statistical significance was set at $P < 0.05$.

3. Results

Three patients were excluded because (1) the central venous catheter was placed at the chosen ICA insonation side while contralateral visualization was poor due to vessel tortuosity, (2) cerebral CO_2 reactivity was not evaluated due to early one-lung ventilation, or (3) use of sevoflurane. Seven patients developed MTS

TABLE 2 Intraoperative data.

	Patients with MTS ($n = 7$)	Patients without MTS ($n = 20$)	*P*-value
Surgical procedure			
Stomach resection, *n* (%)	1 (14%)	11 (55%)	0.0914
Esophageal resection, *n* (%)	6 (86%)	8 (40%)	0.0768
Gastro–entero anastomosis, *n* (%)	0 (0%)	1 (5%)	1
Volume balance from 0 to 90 min after incision			
Crystalloid (l)	0.4 (0.4–0.5)	0.4 (0.4–0.6)	0.7726
Human albumin 5% (l)	0.3 (0.3–0.5)	0.3 (0.0–0.5)	0.3794
Blood loss (l)	0.3 (0.1–0.7)	0.1 (0.0–0.2)	0.0518
Diuresis (l)	0.2 (0.1–0.3)	0.3 (0.1–0.5)	0.5246
Fluid balance (l)	0.0 (−0.1–0.5)	0.3 (0.0–0.5)	0.2981
Vasopressor administration from 0 to 90 min after incision			
Phenylephrine (mg)	0.3 (0.0–0.4)	0.2 (0.0–0.4)	0.768
Noradrenaline (mg)	0.2 (0.1–0.5)	0.2 (0.0–0.4)	0.703

Values are count or median (IQR).

22 [20–26] min after the start of surgery and flushing was level I in all cases. Patient characteristics are reported in Table 1 while the surgical procedure, volume balance, and vasopressor administration during the first 90 min of surgery are reported in Table 2. The patients who developed MTS had a higher weight, height, and body mass index than those who did not develop MTS, while age, gender, and preoperative risk factors were similar. For one patient, surgery was converted from stomach resection to gastro-entero anastomosis due to carcinosis. There was a trend toward a higher incidence of MTS during esophageal- as compared to stomach resection.

At baseline, HR was slightly higher in the patients who later developed MTS (Table 3). HR increased upon flushing and remained elevated for 40 min in patients with MTS, whereas HR increased from 20 to 40 min after incision in the patients without MTS. The increase in HR was greater in the patients with MTS as compared to those without from 0 to 40 min after flushing. After incision and until the end of the study, TPR was reduced in the patients who developed MTS while TPR was reduced only at 20 min after incision in the patients without MTS, and the reduction in TPR was greater in the patients who developed MTS (from flushing until the end of the study). The MAP and SV were stable and similar in the two groups. In contrast, CO increased from 0 to 20 min after flushing while it was maintained in the patients without MTS, but the change in CO was not significantly different in the two groups. Development of MTS led to an increase in SkBF (by 122 PU; 95% CI: 53–191; $P = 0.0007$) upon flushing with an elevation in O_2HB_{skin} from 0 to 20 min after flushing whereas, in patients without MTS, SkBF was maintained while O_2HB_{skin} was stable until it decreased at 60 and 90 min after incision (Figure 1). Skin and muscle oxygenation were unaffected and similar in the two groups whereas HB_{skin} was stable in patients with MTS while HB_{skin} decreased at the end of the study in the patients without MTS.

The S_cO_2 was similar in the two groups and S_cO_2 was stable during surgery until it decreased at the end of the study. There was no significant change in ICA blood flow in response to MTS (by −1 ml/min; 95% CI: −37–35; $P = 0.9529$) as ICA blood velocity, diameter, blood flow, and conductance were similar in the two groups, and were unaffected during surgery. The PaO_2 was lower at baseline in the patients who developed MTS and PaO_2 decreased similarly in both groups from 0 to 20 min after flushing and correspondingly, 20 to 40 min after incision in the patients without MTS (Table 4). The fraction of inspired O_2 was reduced from 40 to 60 min after incision in the patients who did not develop MTS but there was no significant difference in the fraction of inspired O_2 between the two groups, and the arterial saturation was above 92% in all patients throughout the study. There was no difference between the two groups in $PaCO_2$, hemoglobin concentration, and O_2 content, and values were not significantly affected during surgery. Arterial lactate concentration was similar in the two groups, and it increased from 20 to 40 min after flushing and correspondingly from 40 to 60 min after incision in patients without MTS. Infusion of propofol and remifentanil was similar in patients with and without MTS, and the bispectral index was stable. Fluid balance and vasopressor administration were similar in patients with and without MTS, and no patient received red blood cells for the duration of the study. Length of stay was 9 (8–9) days in patients with MTS and 8 (7–10; $P = 0.7986$) days in those without and there was no mortality within 1 month.

4. Discussion

This study in patients planned for stomach- or esophageal-resection evaluated whether MTS affects ICA blood flow. The middle cerebral artery blood velocity is reported to be unaffected by MTS [4], but that observation could be influenced by vasodilation and thus duplex ultrasound was used to evaluate blood flow in the ICA which supplies most of CBF. We found that ICA flow was unaffected by MTS with level I flushing while SkBF and CO became elevated in reflection of a reduction in total peripheral resistance. Furthermore, HR increased while MAP was stable when flushing manifested, as MAP was maintained above 60 mmHg by administration of vasopressors, and there was no significant change in S_cO_2 or skin oxygenation.

MTS likely relates to the release of PGI_2 [2, 3, 9] and in support of maintained ICA flow in response to MTS, administration of PGI_2 to healthy subjects does not affect CBF [10]. The syndrome is generally accompanied by hypotension whereby the effect of MTS on CBF and central hemodynamics may have been attenuated by the administration of vasopressors in the present study. Furthermore, the patients who developed MTS only presented mild flushing which results in smaller hemodynamic changes than MTS with marked flushing [1, 3, 6]. Development of MTS is reported to elevate S_cO_2 likely due to increased SkBF [4]. Here, S_cO_2 was not significantly affected in response to MTS which may reflect the mild degree of flushing and administration of vasopressors [7]. Development of MTS with marked flushing is associated with postoperative complications [1, 23] but MTS appears not to provoke cerebral hyperperfusion.

TABLE 3 Hemodynamic variables in patients who developed mesenteric traction syndrome (MTS) and those who did not.

	Group	Before incision	5 min after incision	Time after flushing/after incision in patients without MTS (min)				*P*-value Time	*P*-value MTS	*P*-value Time∗MTS	*P*-value Time in univariate analysis
				0/20	20/40	40/60	70/90				
Heart rate (bpm)	MTS	67 ± 17	70 ± 11	87 ± 13*†	85 ± 15*†	84 ± 13*†	76 ± 9	<0.0001	0.0079	0.0002	<0.0001
	No MTS	63 ± 9	65 ± 11	70 ± 11†	70 ± 13†	65 ± 11	63 ± 10				<0.0001
Mean arterial pressure	MTS	77 ± 16	61 ± 12	63 ± 13	70 ± 10	69 ± 10	65 ± 11	0.0265	0.9233	0.2947	
(mmHg)	No MTS	68 ± 12	66 ± 10	64 ± 14	70 ± 13	69 ± 10	71 ± 10				
Stroke volume (ml)	MTS	70 ± 11	74 ± 22	78 ± 21	77 ± 20	69 ± 18	72 ± 23	0.3382	0.5937	0.7498	
	No MTS	77 ± 20	80 ± 25	81 ± 26	78 ± 21	80 ± 21	76 ± 16				
Cardiac output (l/min)	MTS	4.5 ± 1.4	4.8 ± 1.4	6.5 ± 1.9†	6.6 ± 2.6†	5.8 ± 2.2	5.4 ± 2.4	<0.0001	0.2476	0.0879	<0.0001
	No MTS	4.7 ± 1.3	5.0 ± 1.5	5.4 ± 1.9	5.4 ± 1.7	5.1 ± 1.5	4.6 ± 1.1				0.0456
Total peripheral resistance	MTS	20 ± 7	15 ± 3†	11 ± 5*†	13 ± 6*†	14 ± 5*†	14 ± 4*†	<0.0001	0.6575	0.0004	0.0001
(mmHg∗min/l)	No MTS	16 ± 5	15 ± 3	13 ± 4†	14 ± 4	15 ± 4	17 ± 4				0.0005
ICA blood flow (ml/min)	MTS	230 ± 50	205 ± 58	225 ± 53	201 ± 44	203 ± 42	185 ± 33	0.0343	0.6384	0.4851	
	No MTS	201 ± 51	203 ± 51	203 ± 69	207 ± 63	191 ± 44	188 ± 41				
ICA TAVMAX (cm/s)	MTS	37 ± 13	32 ± 10	36 ± 13	35 ± 9	35 ± 11	34 ± 11	0.4421	0.864	0.3325	
	No MTS	35 ± 7	36 ± 10	36 ± 10	35 ± 10	36 ± 9	37 ± 13				
ICA diameter (mm)	MTS	6.0 ± 1.0	5.9 ± 1.1	6.0 ± 1.4	5.7 ± 0.9	5.6 ± 1.3	5.4 ± 1.2	0.0019	0.093	0.0535	
	No MTS	5.2 ± 0.6	5.2 ± 0.7	5.2 ± 0.8	5.2 ± 0.7	5.1 ± 0.6	5.1 ± 0.7				
ICA conductance	MTS	3.1 ± 1.0	3.5 ± 1.2	3.7 ± 1.0	2.9 ± 0.9	3.0 ± 1.0	2.9 ± 0.8	0.0002	0.4358	0.4401	
(ml/min/mmHg)	No MTS	3.0 ± 0.6	3.1 ± 0.7	3.2 ± 0.8	3.0 ± 0.6	2.8 ± 0.6	2.7 ± 0.7				
Muscle oxygenation (%)	MTS	78 ± 7	77 ± 7	77 ± 8	77 ± 6	78 ± 8	79 ± 5	0.3306	0.9636	0.1386	
	No MTS	80 ± 9	79 ± 8	77 ± 9	77 ± 10	78 ± 10	77 ± 9				
O_2HB_{skin} (AU)	MTS	21 (17–23)	19 (16–21)	30 (23–33)*†	25 (19–29)*†	23 (15–25)	19 (13–20)	<0.0001	0.7486	0.0072	<0.0001
	No MTS	25 (20–36)	24 (15–31)	24 (20–36)	25 (17–29)	20 (15–30)†	18 (13–21)†				<0.0001
HB_{skin} (AU)	MTS	7 (5–9)	7 (2–10)	7 (6–10)	7 (5–11)	5 (4–10)	5 (4–9)	0.0625	0.4026	0.0108	0.2255
	No MTS	8 (4–12)	7 (3–13)	5 (3–9)	5 (3–7)	4 (3–8)	3 (2–6)†				0.0005

Values are before and 5 min after incision and 0, 20, 40, and 70 min after the start of flushing ($n = 7$) and after 20, 40, 60, and 90 min in patients who did not develop MTS ($n = 20$). Values are mean ± SD or median (IQR). *P*-values represent the overall effect of time point (Time), group (MTS), and the interaction (Time*MTS) as estimated by a repeated measures mixed model. If the interaction of Time*MTS was significant, the effect of Time was evaluated in a univariate repeated measures mixed model. *$P < 0.05$ for the interaction of Time*MTS. †$P < 0.05$ vs. before incision in the analysis of the factor time point. ICA, internal carotid artery; TAVMAX, time-averaged maximum blood velocity; O_2HB_{skin} and HB_{skin} forehead skin oxy- and deoxyhemoglobin concentration.

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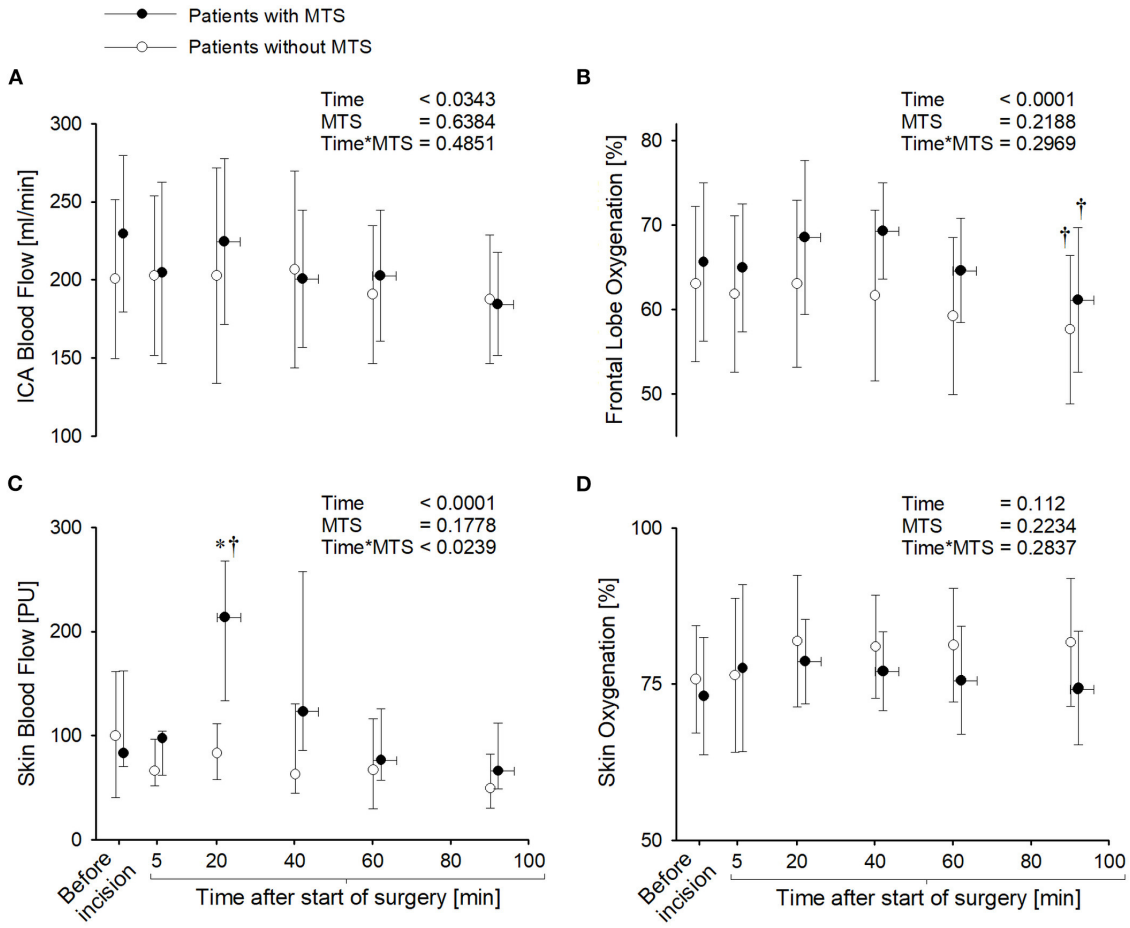

FIGURE 1
Internal carotid artery (ICA) blood flow **(A)**, near-infrared spectroscopy determined frontal lobe oxygenation **(B)**, and forehead skin blood flow and oxygenation **(C, D)** before and 5 min after incision and 0, 20, 40, and 70 min after the start of flushing ($n = 7$) and after 20, 40, 60, and 90 min in patients who did not develop mesenteric traction syndrome (MTS) ($n = 20$). Values are mean ± SD except for skin blood flow which is reported as median (IQR). *P*-values represent the overall effect of time point (Time), group (MTS), and the interaction (Time*MTS) as estimated by a repeated measures mixed model. If the interaction of Time*MTS was significant, the effect of Time was evaluated in a univariate repeated measures mixed model. *$P < 0.05$ for the interaction of Time*MTS. †$P < 0.05$ vs. before incision in the analysis of the factor time point.

The degree of traction on the viscera seems important for the development of MTS as the incidence is reported low in laparoscopic surgery [1] whereas MTS is observed in about 90% of patients when the small intestine is exposed [9]. In our study, the incidence of MTS tended to be lower during stomach, as compared to esophageal resection which could relate to less manipulation of the abdominal viscera during stomach resection. However, similar incidences of MTS of about 50–75% in the two procedures are reported which are higher than in the present study [24]. Patients who developed MTS were taller and with larger body mass index which could relate to more forcible manipulation of the viscera in overweight patients, but the difference may be a chance finding as such differences are not reported [4, 25]. At baseline, the patients who later developed MTS had slightly higher HR and lower arterial O_2 tension despite a similar fraction of inspired O_2 which may be chance findings or could relate to the higher weight of the patients who developed MTS. As none of the patients became hypoxic during the study, we take the difference in arterial O_2 tension to have little influence on the hemodynamic changes. No studies have evaluated the influence of preoperative comorbidities on the incidence of MTS [24] and here we found no differences in age or preoperative comorbidities in the two groups. Propofol anesthesia approximately halves CBF by a reduction in neuronal activity [26, 27] but the infusion of propofol and remifentanil was similar in the two groups of patients, and the bispectral index was stable.

Reperfusion of a grafted liver during orthotopic liver transplantation causes central hemodynamic changes similar to MTS with marked vasodilation, but reperfusion of the transplanted liver also elevates CBF even when the increase in $PaCO_2$ is taken into account [21, 28, 29]. The different cerebrovascular responses may relate to the release of different vasoactive metabolites as reperfusion of a transplanted liver elevates prostaglandin I_2 as observed in MTS but also increases nitrous oxide, endothelin, and thromboxane, in addition to unknown metabolites [30].

4.1. Limitations

The effect of MTS on skin variables and S_cO_2 may have been confounded by vasopressor administration [7] but the administered

TABLE 4 Blood and anesthetic variables in patients who developed a mesenteric traction syndrome (MTS) and those who did not.

	Group	Before incision	5 min after incision	Time after flushing/after incision in patients without MTS (min)				*P*-value Time	*P*-value MTS	*P*-value Time∗MTS	*P*-value Time in univariate analysis
				0/20	20/40	40/60	70/90				
Arterial CO_2 tension (kPa)	MTS	5.6 ± 0.5	5.4 ± 0.3	5.4 ± 0.4	5.4 ± 0.3	5.3 ± 0.2	5.3 ± 0.2	0.4875	0.6571	0.0985	
	No MTS	5.2 ± 0.7	5.3 ± 0.7	5.3 ± 0.7	5.2 ± 0.7	5.3 ± 0.7	5.3 ± 0.9				
Arterial O_2 tension (kPa)	MTS	19 ± 7	16 ± 5	14 ± 4†	15 ± 2†	19 ± 2	23 ± 5	<0.0001	0.008	0.8095	
	No MTS	26 ± 7	23 ± 7	22 ± 7†	21 ± 5†	24 ± 6	29 ± 9				
Arterial hemoglobin (mM)	MTS	7.4 ± 1.1	7.2 ± 1.0	7.4 ± 1.0	7.4 ± 1.0	7.2 ± 0.9	7.1 ± 0.9	0.0167	0.0851	0.4109	
	No MTS	6.6 ± 0.9	6.4 ± 0.9	6.5 ± 0.9	6.6 ± 1.0	6.6 ± 1.0	6.4 ± 0.8				
Arterial O_2 content (mM)	MTS	7.3 ± 1.0	7.1 ± 1.0	7.2 ± 1.0	7.3 ± 0.9	7.2 ± 0.9	7.1 ± 0.9	0.055	0.1028	0.5374	
	No MTS	6.6 ± 0.9	6.4 ± 0.9	6.5 ± 0.9	6.5 ± 1.0	6.6 ± 1.0	6.5 ± 0.7				
Arterial lactate (mM)	MTS	1.2 (1.0–1.2)	1.1 (0.8–1.3)	1.0 (0.8–1.2)	1.1 (0.7–1.2)†	1.0 (0.8–1.2)†	0.9 (0.7–1.2)	0.0108	0.3142	0.9833	
	No MTS	1.0 (0.7–1.3)	0.9 (0.7–1.0)	0.9 (0.7–1.1)	0.8 (0.7–1.1)†	0.8 (0.7–1.1)†	0.8 (0.7–1.1)				
Fraction of inspired O_2 (%)	MTS	43 (42–48)	43 (36–44)	43 (35–45)	43 (42–58)	43 (42–53)	44 (41–53)	0.0892	0.6754	0.0218	0.1512
	No MTS	46 (41–48)	43 (40–46)	43 (39–46)	43 (38–47)†	44 (38–46)†	43 (39–47)				0.0286
Bispectral index	MTS	46 ± 13	43 ± 6	43 ± 6	45 ± 7	44 ± 7	44 ± 5	0.4883	0.5672	0.8517	
	No MTS	42 ± 10	41 ± 9	41 ± 9	43 ± 9	43 ± 10	41 ± 9				
Propofol (μg/kg/min)	MTS	59 (53–64)	65 (53–75)	65 (53–75)	65 (59–75)	65 (59–75)	65 (59–75)	0.5068	0.1845	0.4158	
	No MTS	68 (62–81)	72 (64–84)	71 (64–78)	69 (63–80)	67 (62–80)	68 (62–78)				
Remifentanil (μg/kg/min)	MTS	0.3 (0.3–0.3)	0.3 (0.3–0.4)	0.3 (0.3–0.4)	0.3 (0.3–0.3)	0.3 (0.3–0.3)	0.3 (0.3–0.3)	0.1213	0.2219	0.7824	
	No MTS	0.3 (0.3–0.4)	0.4 (0.3–0.4)	0.3 (0.3–0.4)	0.3 (0.3–0.4)	0.3 (0.3–0.4)	0.3 (0.3–0.4)				

Values are before and 5 min after incision and 0, 20, 40, and 70 min after the start of flushing ($n = 7$) and after 20, 40, 60, and 90 min in patients who did not develop MTS ($n = 20$). Values are mean ± SD or median (IQR). *P*-values represent the overall effect of time point (Time), group (MTS), and the interaction (Time*MTS) as estimated by a repeated measures mixed model. If the interaction of Time*MTS was significant, the effect of Time was evaluated in a univariate repeated measures mixed model. †$P < 0.05$ *vs.* before incision in the analysis of the factor time point.

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doses were similar in the two groups. Laser Doppler flowmetry does not provide an absolute value of SkBF and the study could have benefitted by evaluation using laser speckle contrast imaging [31]. The evaluation of MTS would be improved by the determination of plasma PGI_2, but no cut-off level for the development of MTS is established. The evaluation of ICA flow was unilateral but the contralateral regulation of CBF is similar in response to both propofol anesthesia [26] and administration of, for example, nitroglycerin [32] and L-arginine [33] and we take any difference to be small. We did not evaluate vertebral artery flow which supplies about 20–25% of CBF and may present different regulations from the ICA [34]. The fraction of inspired O_2 was not protocolled but was maintained during the study. We did not evaluate the force of traction or the degree to which the abdominal organs were exposed. The study may have been too small to detect an effect of MTS on cardiac output, ICA diameter, or administration of vasopressors.

4.2. Conclusion

Development of MTS with flushing level I causes vasodilation as observed by a reduction in TPR and increased SkBF but appears not to affect ICA flow.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethical Committee of Copenhagen, Denmark. The patients/participants provided their written informed consent to participate in this study.

Author contributions

NO: conception and design of the study, acquisition, analysis and interpretation of data, and writing of the first draft of the manuscript. AE: acquisition of data and revision of the manuscript. H-JF and LS: design of the study and revision of the manuscript. NS: conception and design of the study, interpretation of data, and revision of the manuscript. All authors have provided final approval of the version to be published and are accountable for all aspects of the manuscript, and including the accuracy and validity of the contents.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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