Original Article

High flow nasal oxygen *vs.* conventional oxygen therapy over respiratory oxygenation index after esophagectomy: an observational study

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Background: Postoperative pulmonary complications after esophagectomy still represent a matter of concern. High flow nasal cannula (HFNC) early after major abdominal and thoracic surgery has demonstrated some advantages over conventional oxygen therapy. Data about respiratory effect of HFNC after esophagectomy is scarce. The primary aim of this study is to investigate if the early use of HFNC after esophagectomy could enhance patients' postoperative respiratory oxygenation (ROX) index and, ultimately, reduce postoperative pneumonia.

Methods: In this single center retrospective study all patients undergoing to esophagectomy for cancer from May 2020 to November 2022 were evaluated. Historical cohort (HC) received postoperative oxygen supplementation with Venturi mask or nasal goggles, and a cohort was put under HFNC (HFNC cohort). ROX index, blood gas analysis, radiological atelectasis score (RAS), post-operative complications' data and information on hospital stay have been collected and analyzed.

Results: Seventy-one patients were included for the final statistical analysis, 31 in the HFNC and 40 in the HC cohort. Mean age was 64±10 years and body mass index (BMI) was 26 [24–29] kg/m^2. ROX index was higher in the HFNC patients than in the HC, 20.8 [16.7–25.9] *vs.* 14.9 [10.8–18.2] (P<0.0001). In the HFNC cohort patients, pH was higher, 7.42 [7.40–7.44] *vs.* 7.39 [7.37–7.43] than HC, while $PaCO_2$ was lower in HFNC cohort compared with HC, 39 [36–41] *vs.* 42 [39–45] mmHg, respectively (P=0.01). RAS was similar between the two cohorts of patients, 1.5±0.98 *vs.* 1.4±1.04 in the HFNC and the HC cohort, respectively (P=0.611). Lower acute respiratory failure (ARF) rate was recorded among HFNC than HC cohort, 0% *vs.* 13% respectively, P=0.06. No difference in pneumonia frequency between two cohorts was shown.

Conclusions: HFNC improved the ROX index after esophagectomy through significant respiratory rate reduction. This tool should be considered for early respiratory support after extubation in this category of

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patients, not only as a rescue therapy for ARF, but also to optimize early postoperative respiratory function. Whether this will improve patients' outcomes requires further large randomized controlled trials.

Keywords: Pneumonia; esophagectomy; high flow nasal cannula (HFNC); post-operative complications; noninvasive respiratory support

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Introduction

The frequency of esophageal cancer has been increasing worldwide, and almost 1 million patients will need esophagectomy by 2040 (1).

These patients are often frail and have suboptimal nutritional status after having undergone neo-adjuvant chemoradiotherapy (CHT-RT) (2). Moreover, they are likely to be exposed to a high rate of perioperative complications (3). Some interventions have been proposed to improve their outcomes, but evidence to support them is still lacking.

On the one hand, according to the Enhanced Recovery After Surgery (ERAS) protocol, a mini-invasive surgical approach with intraoperative protective mechanical ventilation seems to reduce perioperative morbidity (4). On the other hand, postoperative pulmonary complications (PPCs), mainly focusing on pneumonia, represent a significant burden of complications in up to 30% of this population (5). In this regard, noninvasive preventive ventilation (NIV) has been proposed to reduce PPC after extubation, but its role is still being debated (6). Moreover, concerns about possible interference with surgical anastomosis limited the vast NIV application as a standard treatment after extubation (7). Recently, a new noninvasive respiratory device, the high flow nasal cannula (HFNC), has even been widely used in the critical care setting because it increases oxygenation and reduces the need for reintubation in patients considered at high risk (8,9). In addition, it has been shown to produce favorable effects on respiratory function after major abdominal surgery (10). Data on using HFNC after esophagectomy are still scarce (11).

Thus, the primary aim of this pilot study is to investigate if the early use (in the first 24 hours after extubation) of HFNC after esophagectomy could enhance patients' postoperative respiratory function and, ultimately, reduce postoperative pneumonia. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1176/rc).

Highlight box

Key findings
- High flow nasal oxygen after esophagectomy improved blood gas analysis and respiratory oxygenation index, particularly reducing respiratory rate.

What is known and what is new?
- High flow nasal oxygen after cardiac, thoracic or major abdominal surgery reduces the need for reintubation.
- This study highlights the role of high flow nasal cannula (HFNC) after esophagectomy especially as it concerns postoperative respiratory function improvement.

What is the implication, and what should change now?
- Early application of HFNC after esophagectomy ameliorates respiratory parameters. Large randomized trials are warranted to establish if this improvement would translate into a reduced postoperative pulmonary complication rate.

Methods

Setting and design

We studied all consecutive adult patients from May 2020 to November 2022 who underwent esophagectomy at University Hospital of Udine, a high-volume center in the north-east of Italy in Friuli Venezia Giulia Region. Despite ongoing COVID-19 pandemic, we continued to deliver appropriate care after reorganization the care path at our hospital (12). Notwithstanding, a 20% volume reduction in esophagectomy was noted.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This observational retrospective study was conducted after it received the Institutional Review Board of the University of Udine's approval (No. #176-2022). Each patient's willingness to participate was obtained through a signed general informed consent for research purposes G.E.C.O. European General Data Protection Regulation 2016/679 (G.D.P.R.) was respected. The same standard of care was applied to all patients admitted to the postanesthesia care unit.

Inclusion and exclusion criteria

Inclusion criteria were (I) all adult patients underwent esophagectomy for cancer with radical intent and (II) all were receiving an open or mini-invasive surgical approach extubated within 4 hours after the end of surgery. We excluded patients who (I) underwent esophagectomy combined with other types of surgery (lung or hepatic resection), (II) received esophagectomy with palliative intent, (III) with previous SARS-CoV2 infection, (IV) with incomplete data, and (V) with severe end-stage organ disease (liver cirrhosis, kidney failure under renal replacement treatment or patient awaiting solid organ transplant).

Surgical characteristics

Minimally invasive McKeown esophagectomy was performed with the technique described in our previous publication (13) with patients in a prone position and single-lumen endotracheal intubation. The hybrid approach (laparoscopy/thoracotomy) was the preferred technique for the Ivor-Lewis esophagectomy. In McKeown minimally invasive esophagectomy (MIE), the mediastinal pleura and pulmonary ligament were divided. Moreover, the azygos vein was isolated. Subsequently it was divided at the level of its arc using a vascular stapler. Esophageal dissection with periesophageal tissue and *en bloc* lymphadenectomy were performed using a coagulating hook caudally to the diaphragmatic hiatus and cranially to the pleural dome. The gastric conduit was created by multiple firings of stapler. The celiac lymph nodes were dissected. Left cervicotomy was performed, and the upper esophagus was isolated and divided. A cervical end-to-side anastomosis was performed using a circular stapler. In Ivor-Lewis procedure, right thoracotomy was performed after celiac lymphadenectomy and gastric conduit creation. The azygos vein was isolated and divided as previously described; esophageal dissection was performed cranially to the azygos arc. The esophagus was then divided and a purse-string was made in the proximal esophageal stump with a Prolene 2/0; the anvil of a circular stapler was introduced into the esophageal stump. An intrathoracic esophago-gastric anastomosis was then performed. After esophagectomy one or two chest tubes were left in the thorax. In all patient we performed an indocyanine green fluorescence near infrared lymphography to obtain the visualization of the thoracic duct (14).

The pleural cavity was drained with a chest tube and trans-hiatal Jackson-Pratt drain.

Preoperative phase

All patients underwent preoperative evaluation following the European Society of Anaesthesiology (ESA)/European Society of Cardiology (ESC) guidelines (15). A dedicated dietician performed the preoperative nutritional plan. Pulmonologists and physiotherapists evaluated patients at least one month before surgery, performing respiratory functionality tests and respiratory prehabilitation with a primarily educational objective.

Intra-operative phase

All patients were monitored with electrocardiography, noninvasive arterial blood pressure, and SpO_2.

After anesthesia induction with propofol, fentanyl or remifentanil, and rocuronium, the trachea was intubated with a single or, if needed, a double-lumen tube. Mechanical ventilation was set at 6 mL/kg of tidal volume (TV) to maintain SpO_2 ≥92% and end-tidal CO_2 ($ETCO_2$) between 35–45 mmHg. Under ultrasound guidance, a radial artery and central venous line were put in place, and a urinary catheter with a temperature probe completed the intraoperative patient's monitoring.

Anesthesia was maintained with sevoflurane/desflurane or total intravenous anesthesia (TIVA) per the anesthesiologist's preference and the patient's history.

After thoracic procedure ended, lung recruitment maneuvers have been performed.

At the end of the surgery, a nasogastric tube was placed with the surgeon's guidance and left in place until dietary intake was sufficient.

Nonsteroidal anti-inflammatory drugs, opioids, and paracetamol were used for postoperative analgesia.

Postoperative care

Patients with hemodynamic stability, normothermia, complete reversal of neuromuscular block, and standard arterial blood gas analysis were extubated within 4 hours after end of surgery in the operating room or intensive care unit (ICU). Nasogastric tube decompression was maintained until the contrast swallow study on a postoperative day (POD) 7; early mobilization and physiotherapy were started in POD 1; chest tube was removed within 96 hours and when output <100 mL/die. After the swallow study, an oral diet was started.

Chest physiotherapy and oxygen supplementation

On the 1st POD, patients were placed under the care of respiratory physiotherapists. The goals of postsurgical respiratory physiotherapy were to help mucociliary clearance (preventing accumulation and facilitating the removal of excess bronchial secretions), prevent atelectasis, improve the ventilation-to-perfusion ratio, and improve gas exchange. After extubation, patients received oxygen supplementation per our routine practice to maintain SpO_2 ≥92%. After a feasibility study to improve the learning curve in using HFNC (AIRVO2, Fisher and Paykel Healthcare, New Zealand) after esophagectomy in surgical wards (16), from May 2021, it has been systematically applied to all patients for 24 hours after extubation. We decided to apply humidified HFNC at a flow rate of 50 L/min when body weight was <80 kg and 60 L/min in case of ≥80 kg of body weight. If not tolerated, we reduced the gas flow by 5 L/min until the patient's comfort was obtained. Large-bore cannulas were of adequate size based on nostril dimensions. We initially set 34–37 ℃ of gas temperature according to the patient's tolerance. Oxygen enrichment was used to obtain SpO_2 >92–98%. In contrast, the historical cohort (HC) of patients (May 2020–May 2021) received humidified O_2 with a Venturi mask or nasal googles to achieve the same oxygenation targets. In the case of acute respiratory failure (ARF), we used a different form of respiratory support as an escalation approach: conventional oxygen therapy (COT)→HFNC→continuous positive airway pressure (C-PAP)/NIV→endotracheal intubation.

Data collection

Age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, Charlson Comorbidity Index (CCI), Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score (17), preoperative weight loss, preoperative nutritional support (PreOp NS), preoperative oncological data [type of tumor, site, clinical tumor-node-metastasis (cTNM) VIII edition radiation, chemotherapy (CHT) or CHT-RT] and surgical data [type of surgery (open *vs.* minimally invasive-MIE), length of surgery] were considered. Intraoperative anesthesiological data included the total amount of fluids, TV during the abdominal and thoracic phase, positive end-expiratory pressure (PEEP), and use of TIVA. Respiratory parameters immediately after extubation included respiratory rate (RR), FiO_2, SpO_2/FiO_2, respiratory oxygenation (ROX) index (18). In addition to the same parameters, 24 hours after extubation, blood gas analysis (pH, pO_2, pCO_2) were also collected. Data on hospital stay and mortality at 30- and 180-day after surgery were also collected.

Postoperative complications

We defined postoperative complications according to the International Consensus on Standardization of Data Collection for Complications Associated with Esophagectomy published by the Esophagectomy Complications Consensus Group (19).

ARF was defined as PaO_2 ≤60 mmHg while breathing room air and/or $PaCO_2$ >50 mmHg in patients with normal preoperative blood gas analysis, with the presence of dyspnoea or tachypnoea (RR >20 apm).

An expert radiologist (L.C.) with over 10 years of experience and dedicated to chest imaging, blinded to patient clinical data, reviewed the chest X-rays for atelectasis between the 2nd and 4th POD according to the score developed by Richter Larsen *et al.* (20). In detail, the radiological atelectasis score (RAS) is a numerical scale from 0 (clear lung fields) to 4 (bilateral lobar atelectasis) that defines the entity of atelectasis.

Primary outcome

The study's primary outcome was to assess if the early use of HFNC, compared with COT after esophagectomy improves respiratory gas exchange and ROX index 24 hours after extubation.

Secondary outcome

The secondary outcomes were to evaluate RAS score in the cohorts of patients and observe the frequency of postoperative complications.

Statistical analysis

Continuous data were presented as mean ± standard deviation or median [interquartile range (IQR)] according

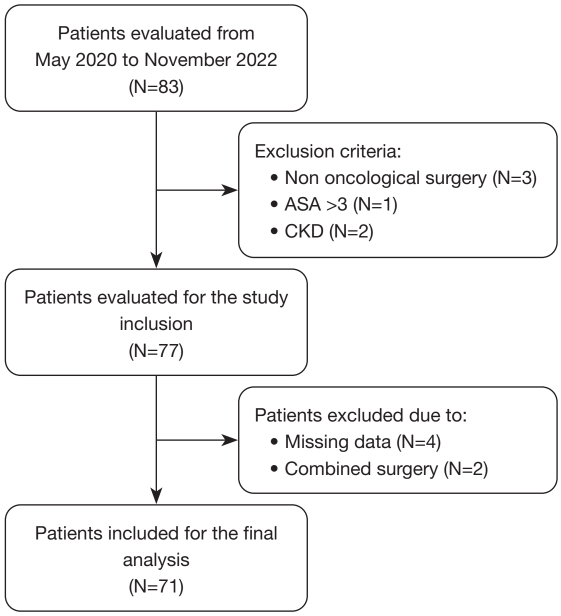

Figure 1 Study flow-chart. ASA, American Society of Anesthesiologists; CKD, chronic kidney disease.

to the normality of the distribution tested with the Shapiro-Wilk test. Categorical variables were expressed as absolute values and relative frequencies. Comparison between continuous variables was done with *t*-test or *U*-Mann-Whitney as appropriate. Chi-square or Fisher's exact test was applied to examine any differences between categorical variables. The level of statistical significance was set at $P<0.05$. No imputation was done for missing data. Considering an expected increase in the ROX index by 30% (*t*-test between two independent means) in the HFNC cohort after our preliminary results (16), with $\alpha = 0.05$ and $\beta = 0.90$, 27 patients needed to be enrolled per cohort. Statistical analysis was performed with R software and GraphPad Prism v. 9.0.

Results

During the study period, 83 esophagectomies were performed in our center. Seventy-one patients were included in the final data analysis, as the study flow chart (*Figure 1*) shows. Thirty-one patients represent the HFNC cohort, while the remaining 40 patients represent the HC. This last cohort included patients who underwent esophagectomy from May 2020 to May 2021 until the sample size was reached.

Patients were mainly men (90%) with a mean age of 64±10. Most patients were classified as having an ASA 2 score (54%). All patients can be considered at high risk (42.1% risk) of PPCs according to ARISCAT score.

Comparisons between patients' baseline characteristics in HFNC and the HC showed no significant differences (*Table 1*).

Adenocarcinoma was the most frequent histological type of cancer (72%) in the lower third part of the esophagus (85%), as shown in *Table 2*.

Fifty-three patients (75%) underwent the open Ivor-Lewis approach (*Table 3*).

The HC showed a shorter duration of surgery ($P<0.01$). No significative difference among intraoperative anesthesiological data was revealed when comparing the two cohorts except regarding the lower PEEP level in the control than in the HFNC cohort, $P=0.04$ (*Table 3*).

ROX index was similar just after extubation in the two cohorts, 13.8 [IQR, 12.8–15.6] *vs.* 13.7 [IQR, 12–15.4] in HFNC and HC cohort respectively ($P=0.547$).

Higher ROX index value was recorded 24 hours after extubation in HFNC than HC cohort, 20.8 [IQR, 16.7–25.9] *vs.* 14.9 [IQR, 10.8–18.2] respectively ($P<0.0001$) as shown in *Figure 2*.

RR was significantly lower 24 hours after extubation in HFNC than HC cohort, 15 [IQR, 13–18] *vs.* 21 [IQR, 18–23] apm ($P<0.0001$) respectively.

Regarding blood gas analysis, in the HFNC cohort patients' pH was higher, 7.42 [IQR, 7.40–7.44] *vs.* 7.39 [IQR, 7.37–7.43] ($P<0.001$), than HC, and $PaCO_2$ was lower in HFNC cohort compared with HC, 39 [IQR, 36–41] *vs.* 42 [IQR, 39–45] mmHg, respectively ($P=0.01$), as shown in *Figure 3*.

The mean flow delivered through HFNC was 47±6 L/min at a median temperature of 34 [IQR, 31–37] ℃. In most cases (65%), patients tolerated the prescribed gas flow rate. In the remaining (35%), gas flow or temperature was reduced to achieve the patients' comfort.

RAS was similar between the two cohorts of patients, 1.5±0.98 *vs.* 1.4±1.04 in the HFNC and the HC cohort, respectively ($P=0.611$).

A lower postoperative respiratory complication was found in the HFNC patients than in the HC patients regarding pneumonia and anastomotic leak, even though it did not reach statistical significance (*Table 4*).

A higher rate of ARF was registered among the HC cohort than in the HFNC, 13% *vs.* 0% ($P=0.06$), see *Table 5*. The five patients to whom ARF was diagnosed developed low oxygen saturation (SpO_2 <92%) after 46 [IQR, 40–54]

Table 1 Baseline characteristics of patients

Characteristics	Overall (n=71)	HFNC (n=31)	HC (n=40)	P value
Male (%)	90	93	88	0.65
Age (years)	64±10	63.9±9	64.1±11	0.71
BMI (kg/m^2)	26 [24–29]	26 [24–29]	27.5 [25–30]	0.16
ASA score				0.08
1	3 [4]	0	3 [8]	
2	38 [54]	14 [45]	24 [60]	
3	30 [42]	17 [55]	13 [33]	
CCI	4 [3–5]	4 [3–6]	5 [3–6]	0.80
ARISCAT score	50 [50–50]	50 [50–50]	50 [50–50]	0.70
SpO_2/FiO_2	461 [447–471]	461 [447–466]	462 [461–471]	0.60
PreOp weight loss (% of BW)	10 [6–18]	10 [5–14]	10 [6–19]	0.32
PreOp NS	38 [54]	16 [52)	22 [55]	0.50

Data are expressed as mean ± standard deviation, percentage/absolute frequency and percentage [%] or as median and interquartile ranges [25–75]. HFNC, high flow nasal cannula cohort; HC, historical cohort; BMI, body mass index; ASA, American Society of Anesthesiologists; CCI, Charlson's Comorbidity Index; ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; PreOP, preoperative; BW, body weight; NS, nutritional support.

Table 2 Pre-operative oncological data

Pre-operative data	Overall (n=71)	HFNC (n=31)	HC (n=40)	P value
Type of tumor, n [%]				0.43
ADK	51 [72]	24 [77]	27 [68]	
SCC	20 [28]	7 [23]	13 [33]	
Site, n [%]				0.42
Middle	11 [15]	6 [19]	5 [13]	
Lower	60 [85]	25 [81]	35 [88]	
cTNM VIII edition, n [%]				0.36
I	3 [4]	2 [6]	1 [3]	
II	6 [8]	3 [10]	3 [8]	
III	60 [85]	25 [81]	35 [88]	
IV	2 [3]	1 [3]	1 [3]	
CHT neo, n [%]	21 [30]	10 [32]	11 [28]	0.79
CHT-RT neo, n [%]	39 [55]	20 [65]	19 [48]	0.15

HFNC, high flow nasal cannula cohort; HC, historical cohort; ADK, adenocarcinoma; SCC, squamous carcinoma; cTNM, clinical tumor-node-metastasis; CHT, chemotherapy; neo, neoadjuvant; CHT-RT, chemoradiotherapy.

Table 3 Main surgical and anesthesiological intraoperative data

Intraoperative data	Overall (n=71)	HFNC (n=31)	HC (n=40)	P value
Type of surgery				0.72
Open Ivor-Lewis	53 [75]	23 [74]	30 [75]	
MIE Ivor-Lewis	2 [3]	0	2 [5]	
Open McKeown	3 [4]	2 [6]	1 [3]	
MIE McKeown	13 [18]	6 [19]	7 [18]	
Length of surgery (min)	305 [240–350]	330 [280–370]	267 [230–341]	<0.01
Total IOP fluids (mL)	3,500 [3,000–4,460]	3,500 [2,300–4,500]	3,200 [2,550–4,000]	0.28
IOP fluid balance (mL)	1,550 [725–2,238]	1,850 [1,050–2,438]	1,500 [625–2,150]	0.21
TV_{ABD} (mL/kg IBW)	7.6 [7.2–8.1]	7.6 [7–8]	7.6 [7.4–8.4]	0.27
TV_{THOR} (mL/kg IBW)	5.5 [4.8–6.2]	5.5 [4.6–6.1]	5.6 [5–6.2]	0.13
$PEEP_{ABD}$ (cmH_2O)	5 [5–5]	5 [5–6]	5 [5–5]	0.84
$PEEP_{THOR}$ (cmH_2O)	5 [4–6]	5 [3–5]	5 [5–7]	0.04
TIVA	6 [8]	3 [10]	3 [8]	0.74

Data are expressed as absolute frequency and percentage [%] or as median and interquartile ranges [25–75]. HFNC, high flow nasal cannula cohort; HC, historical cohort; MIE, minimally invasive esophagectomy; IOP, intraoperative; TV, tidal volume; ABD, abdominal phase; IBW, ideal body weight; THOR, thoracic phase; PEEP, positive end-expiratory pressure; TIVA, total intravenous anesthesia.

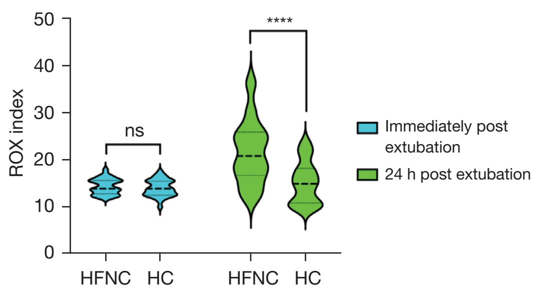

Figure 2 ROX index immediately and 24 hours after extubation. In the left part (light blue box violin plot), ROX index was similar just after extubation in the two cohorts. On the opposite, 24 hours after extubation (light green box violin plot) ROX index was higher in the HFNC than HC cohort. ns, not significant; ****, P<0.0001. HFNC, high flow nasal cannula cohort; HC, historical cohort; ROX, respiratory oxygenation.

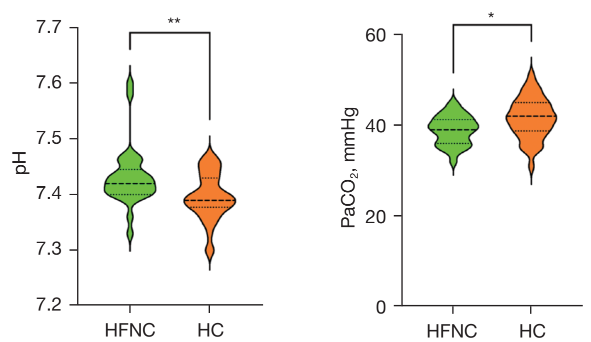

Figure 3 Blood gas analysis at 24 hours after extubation. pH was higher and PaCO2 lower in HFNC cohort than HC cohort. *, P=0.01; **, P<0.001. HFNC, high flow nasal cannula cohort; HC, historical cohort.

hours from extubation. Bacterial pneumonia was diagnosed in three of them, and antibiotic treatment improved the condition. For the remaining two patients, a negative computed tomography (CT) scan ruled out pulmonary embolism but revealed large right atelectasis, so fiberoptic bronchoscopy revealed bronchial obstruction due to secretions with subsequent improvement after their removal.

One required reintubation and mechanical ventilation for 7 days, and four cases were treated with HFNC lasting 3 [IQR, 2–4] days.

Median length of hospital stay (LOS_{HOSP}) was 15 [IQR, 12–20] days in both groups. No death was registered at the 180-day follow-up (*Table 5*).

Table 4 Post-operative complications

Complications	Overall (n=71)	HFNC (n=31)	HC (n=40)	P value
Overall, n [%]	35 [49]	15 [48]	20 [50]	0.89
Pulmonary[†], n [%]	18 [25]	8 [26]	10 [25]	0.93
Pneumonia	15 [21]	6 [19]	9 [23]	0.74
Drained pleural effusion	3 [4]	1 [3]	2 [5]	0.73
PNX requiring drainage	2 [3]	1 [3]	1 [3]	0.86
ARF	5 [7]	–	5 [13]	0.06
Cardiovascular, n [%]	13 [18]	6 [19]	7 [18]	0.84
AF	11 [15]	5 [16]	6 [15]	0.90
CA	1 [1]	1 [3]	–	–
PE	1 [1]	–	1 [3]	–
Surgical, n [%]	8 [11]	3 [10]	5 [13]	0.71
Anastomotic leak	7 [10]	2 [6]	5 [13]	0.40
Vocal cord paralysis	1 [1]	1 [3]	–	–
Infectious, n [%]	7 [10]	2 [6]	5 [13]	0.72

[†], the number of pulmonary complications represents each single patient with at least one pulmonary complication. However, some patients experienced more than one complication. For this reason, while listing all complication, the sum does not equal to the number reported in pulmonary. HFNC, high flow nasal cannula cohort; HC, historical cohort; PNX, pneumothorax; ARF, acute respiratory failure; AF, atrial fibrillation; CA, cardiac arrest; PE, pulmonary embolism.

Table 5 Post-operative and hospital data

Hospital data	Overall (n=71)	HFNC (n=31)	HC (n=40)	P value
LOS_{ICU} (days)	1 [1–2]	1 [1–2]	1 [1–3]	0.40
LOS_{HOSP} (days)	15 [12–20]	15 [13–19]	15 [12–22]	0.97
Food intake (days)	10 [8–14]	11 [9–14]	10 [8–13]	0.38
30-day mortality	0	0	0	–
180-day mortality	0	0	0	–

Data are expressed as median and interquartile ranges [25–75] or percentage (%). HFNC, high flow nasal cannula cohort; HC, historical cohort; LOS_{ICU}, length of ICU stay; ICU, intensive care unit; LOS_{HOSP}, length of hospital stay.

Discussion

The main finding of this study is that early application of HFNC after esophagectomy significantly improved blood gas analysis and ROX index. At the same time, the effect of HFNC on postoperative atelectasis reduction is negligible.

Esophagectomy still carries a high rate of postoperative complications, and early extubation after esophagectomy remains a matter of debate (21). Although prolonged invasive mechanical ventilation can lead to higher rates of pneumonia and barotrauma, early ARF after extubation with reintubation significantly worsens patients' outcomes (22). Moreover, patients who underwent esophagectomy are considered at high risk of reintubation (23). A supportive tool that mediates between these opposite situations is consequently advocated. Evidence from large randomized trials in major abdominal, thoracic, and cardiac surgery has highlighted the possible benefits from early post-extubation application of HFNC in terms of reduced need for reintubation and LOS_{HOSP} (24). However, substantial evidence in the specific setting of esophageal surgery needs to be better documented. Xia and colleagues analyzed the effect of HFNC in the setting of post-esophagectomy ARF. In their retrospective study they found that HFNC improved hypoxemia, increased the flow sputum and reduced post-operative pulmonary complications (25).

From a pathophysiological point of view, the anticipated benefits of the application of HFNC are (I) delivery of heated and humified gas with improved secretions clearance and (II) increased dead space washout and support of a low level of PEEP (26). The net effect of these mechanisms of action should sustain improvements in some critical patients, which could decrease atelectasis, increase oxygenation, improve CO_2 elimination with reduced RR, and reduce inspiratory effort and work of breathing, finally reducing dyspnea and ameliorating clinical outcomes (27). All these benefits are desirable after esophagectomy, but they need to be proven. We found that in patients treated with HFNC, the level of $PaCO_2$ was significantly lower than in the HC group, with a consequently higher pH value. Moreover, patients demonstrated a significantly lower RR in the HFNC cohort. As a final result, the ROX index was considerably higher in the HFNC cohort (20.8 *vs.* 14.9, P<0.0001) than the HC one. Our results support the HFNC effect of more efficient dead space washout (26).

In a recent physiologic study, Mauri *et al.* demonstrated that ROX index increase depends on the flow rate set with HFNC, highlighting how higher values were reached at higher flow rates (28). For practical reasons, we chose to deliver 50 or 60 lt/min according to the patient's body weight. At this point, we should consider that HFNC often requires temperature and flow rate adjustments to achieve the patient's comfort and tolerance. In our study, 65% of patients tolerated the set flow rate, while the remaining required lower than predefined values due to poor tolerability. Higher flow rates are probably better tolerated by ARF patients, such as the critically ill, who immediately feel the benefit. In contrast, the lower tolerance observed in this study could reflect the better oxygenation of this postoperative category of patients. Although the ROX index has been validated for reintubation risk prediction after the institution of HFNC, it can be considered a global compound of respiratory function (29).

Postoperative patients with less RR and better oxygenation, i.e., lower work of breathing, could perform physiotherapy and mobilization sooner and better, speeding up the recovery phase.

A recent meta-analysis demonstrated that postoperative rehabilitation resulted in a lower incidence of pneumonia, a shorter LOS_{HOSP}, and better health related quality of life scores for dyspnea and physical functioning (30).

However, this was not the main focus of this study and was not properly investigated.

Pulmonary complications after esophagectomy are supposed to be caused by atelectasis (31). Many factors contribute to developing atelectasis after esophagectomy: intraoperative one-lung ventilation, pneumoperitoneum or induced pneumothorax, mediastinal dissection, and the necessity of lung retraction to optimize esophageal exposure. Indeed, some postoperative factors also increase the risk of their formation, such as diaphragmatic dysfunction with consequent impaired cough, pain, and reduced ability to clear tracheobronchial secretions. In addition, esophagectomy comprehends abdominal and thoracic cavity access, with all the consequent complications of both these types of major surgery. Atelectasis occurs 24–72 h after surgery with various degrees of clinical signs, from mild to severe symptoms of respiratory failure requiring endotracheal intubation and mechanical ventilation (32). Consequently, applying HFNC theoretically should reduce atelectasis formation through the delivery of low levels of PEEP. However, we were not able to demonstrate this in our study. RAS score was similar in the two cohorts of patients. We acknowledge that the RAS score has limitations, and a CT scan would be the examination of choice. However, a chest X-ray is sufficiently useful after esophagectomy unless a clinical scenario requires other image modalities. Moreover, it implies lower radiation exposure than a CT scan. This finding carries two considerations: atelectasis probably is not the sole hit that leads to PPCs, and, secondly, PEEP generated by HFNC could not be sufficient to reopen closed alveoli within atelectasis (33). This last point is a matter of debate. If some evidence supports that HFNC, especially at high flow rates, produces PEEP near 5 cmH_2O, simply opening the mouth decreases the PEEP level at lower values (about 1 cmH_2O), making improbable a net effect or alveolar recruitment (34). Moreover, it cannot be excluded that besides recruitment in dependent lung regions, HFNC could also overdistend the nondependent parts without oxygenation improvement (35). More evidence is needed in this regard. Evidence highlights that postoperative complication worsens patient outcomes (36).

But it is not surprising that the overall complication rate reached 49%. In a recent benchmarking study from the Esophageal Complications Consensus Group (ECCG)'s large database (ESODATA), 59% of patients developed postoperative complications, with PPC the most represented group (27.8% in 1,595 patients) (37,38).

Patients undergoing esophagectomy have many concomitant risk factors for postoperative complications. Pre-operative ones such as nutritional status or neoadjuvant CHT-RT, intraoperative factors like fluid administration and mechanical ventilation, and postoperative ones such as adequate mobilization can all contribute to the patient's outcome (39). Moreover, it is difficult to extrapolate a single factor that, *per se*, could influence a patient's outcome. In this regard, HFNC is part of a continuum of care that has been demonstrated to improve postoperative pulmonary function in this study. Even though we did not record significant differences in terms of PPC between groups, it is worth noting that no reintubation within 7 days nor ARF has been observed in the HFNC cohort of patients, while 5 (13%) patients in the HC had an ARF (P=0.06). Whether the systematic application of HFNC early after esophagectomy will improve outcomes still needs to be determined. In this regard, an ongoing randomized multicenter study (NCT05718284) will produce more data and evidence on this important topic with a strong physiological basis.

This study has some limitations. First, its retrospective design limits some argumentations, and the lack of randomization carries selection biases. Second, this is a single-center study, so generalizability could be questioned. Third, we did not record the tolerability of HFNC after 24 hours, but this was not the topic of this preliminary study because it was already explored in a pilot study, as was previously mentioned. Consequently, we cannot exclude that if higher rates had been delivered, some additional benefit could have further ameliorated postoperative outcomes.

Conclusions

In conclusion, HFNC improved the oxygenation index after esophagectomy. This tool should be considered for early respiratory support after extubation in this category of patients, not only as a rescue therapy for ARF, but also to optimize early postoperative respiratory function. Whether this will improve patients' outcomes requires further large randomized controlled trials.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1176/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This observational retrospective study was conducted after it received the Institutional Review Board of the University of Udine's approval (No. #176-2022). Each patient's willingness to participate was obtained through a signed general informed consent for research purposes G.E.C.O. and the European General Data Protection Regulation 2016/679 (G.D.P.R.) was respected.

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