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Research Article

The Predictive Value of Diaphragm Thickness Fraction on Postoperative Pulmonary Complications after Digestive Cancer Curative Surgery

Oussama Ssouni[1]*, Abdelilah Ghannam[1], Brahim El-Ahmadi[1], Zakaria Belkhadir[1], Khalid Abidi[2], Amal Bouziane[3,4] and Redouane Abouqal[4,5]

[1]Department of intensive care, National Institute of Oncology, Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco

[2]Medical Intensive Care Unit, Ibn Sina Hospital, Mohammed V University in Rabat, Morocco

[3]Department of Periodontology, Faculty of Dental Medicine, Mohammed V University in Rabat, Morocco

[4]Laboratory of Biostatistics, Clinical Research, and Epidemiology, Mohammed V University in Rabat, Morocco

[5]Acute Medical Unit, Ibn Sina University Hospital, Rabat, Morocco

More Information

***Address for correspondence:**
Oussama Ssouni, Department of intensive care, National Institute of Oncology, Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco,
Email: ssounioussama@gmail.com

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Keywords: Postoperative pulmonary complications; Digestive cancer curative surgery; Diaphragm thickness fraction; Ultrasonography

Abstract

Background: Postoperative Pulmonary Complications (PPCs) escalate mortality, hospitalization, and costs. This study aimed to predict PPCs after curative digestive cancer surgery using thickness fraction (TF_{di}) determined by ultrasonography.

Methods: A prospective study was conducted over a period of 9 months. Diaphragmatic ultrasound was performed pre-surgery and repeated postoperatively (within 24 hours of ICU admission, then day 3). Right and left hemidiaphragm thickness at end-expiration (T_{EE}) and peak-inspiration (T_{PI}) were measured using ultrasonography. The maximal diaphragm thickening fraction during inspiration ($TF_{di,max}$) was calculated: $TF_{di,max} = (T_{PI} – T_{EE})/T_{EE}$. Patients were classified into No-PPCs and PPCs groups.

Results: 159 patients participated, 55 (34.6%) developed PPCs. ICU stay was longer in PPCs patients with more deaths. $TF_{di,max}$ decreased postoperatively and remained lower in PPCs patients [44.83% ± 11.07 *vs.* 31.54% ± 8.45; $p < 0.001$]. The receiver operating characteristic curve yielded an area under the curve of 0.83 [95% IC: 0.754 – 0.887]. $TF_{di,max} < 37\%$ had 72.7% sensitivity (95% IC: 59.0% – 83.8%) and 80.8% specificity (95% IC: 71.8% – 87.8%), Positive and negative Likelihood Ratios were 3.7 (95% IC: 2.4 – 5.7) and 0.3 (95% IC:0.2 – 0.5), respectively. In multiple logistic regression, preoperative risk factors for PPCs included $TF_{di,max} < 37\%$ [OR: 7.10; 95% CI: 1.71 – 18.60; $p < 0.001$] and supramesocolic surgery [OR: 9.94; 95% CI: 3.62 – 27.29; $p < 0.001$]. Epidural administration was protective [OR: 0.21; 95% CI: 0.052 – 0.87; $p = 0.031$].

Conclusion: A low preoperative $TF_{di,max}$ identifies high-risk PPCs patients after digestive cancer surgery, aiding targeted preventive strategies like inspiratory muscle preoperative training.

Introduction

Epidemiology

Postoperative Pulmonary Complications (PPCs) significantly escalate mortality and contribute to extended hospital stays, leading to increased costs [1]. The definition of PPCs has varied across literature, with the one proposed by Pedersen et al being a particularly suitable one. It encompasses any lung abnormality that results in identifiable lung disease or dysfunction, necessitating medical intervention, and adversely affecting a patient's clinical progression. This comprehensive definition encompasses atelectasis, lung infections, respiratory failure, prolonged mechanical ventilation, exacerbation of underlying sub-respiratory disease, and bronchospasm [2]. The incidence of PPCs in major surgery spans a range from <1% to 23% [3-10]. Notably, pulmonary complications surpass cardiac complications in prevalence [11-13], with postoperative respiratory failure being the most frequent PPC [10-14]. Patients with PPCs face increased short-term and long-term mortality, with a significant portion (14% - 30%) succumbing within 30 days post-major surgery compared to 0.2% - 3% without PPCs [6,7,9,15-17]. Long-term data from observational studies reveal substantial disparities in mortality rates between patients with and without PPCs: 45.9% *vs.* 8.7% at 1 year and 71.4% *vs.* 41.1% at 5 years [17]. PPCs also heighten morbidity, extending hospital stays by 13 - 17 days [9,11,18]. Instances such as postoperative respiratory failure necessitating unplanned re-intubation, typically within 72 hours of surgery [16,19], significantly amplify morbidity and length of hospital stay [16,18]. The occurrence of PPCs escalates healthcare costs primarily due to prolonged hospital stays [1].

Impact on surgery

A substantial majority of PPCs, about 85%, manifest within the initial three postoperative days [20]. This occurrence is partly attributed to early postoperative pathophysiological reductions in lung volumes [21], which, if prolonged, can lead to severe atelectasis, hypoxemia, and pneumonia [22,23]. The strength of respiratory muscles has been suggested to play a role in the development of certain PPCs [24,25]. Post-surgery, patients must cope with increased respiratory workload, reopen areas of lung atelectasis, and generate an effective cough to mobilize secretions. Interventions that fortify respiratory muscles before surgery and reduce their workload afterward have demonstrated benefits in randomized controlled clinical trials for PPC prevention [21,25-27]. The diaphragm, the primary respiratory muscle, can be assessed by measuring its thickness fraction (TFdi) at the attachment zone using ultrasound [28]. TFdi has shown reliability [29] and validation against trans-diaphragmatic pressure measurements [30], and is a strong predictor of successful mechanical ventilation weaning [31,32]. The potential of this diaphragmatic function marker was assessed by Cavayas and colleagues in cardiac surgery [33-35]. However, no prior study has explored the value of TFdi,max in a specific perioperative context, specifically digestive cancer curative surgery. Thus, our study aims to evaluate the diagnostic performance of preoperative ultrasound measurement of maximum TFdi for predicting PPCs in patients undergoing digestive cancer curative surgery.

Materials and methods

Study design and settings

We conducted a prospective cohort study at the National Institute of Oncology in Rabat, Morocco. It is an academic center encompassing several specialties (medical oncology, ICU, radiotherapy, radiology, and digestive cancer surgery). The patients followed in this establishment are mainly affected by malignant diseases. The duration of the study was approximately nine months, between May 2019 and January 2020. Participants were recruited during the 48 hours before performing the surgery.

Participants

Patients 16 years of age or older undergoing digestive cancer curative surgery (laparotomy or laparoscopy) were eligible for inclusion in the study. The exclusion criteria were: urgent surgery, the existence of a pre-existing neuromuscular pathology, and the need for preoperative ventilatory support.

Diaphragm thickness fraction

Diaphragmatic ultrasound was performed 24 to 48 hours before digestive cancer curative surgery, during the patient's hospitalization period in the surgical department, then repeated postoperatively (within 24 hours after his admission to intensive care, and on day 3). The patient was placed in a semi-seated position with the headboard at 45 degrees. Postoperative analgesia has been systematically optimized using a Visual Analog Scale (VAS), with the objective of a VAS <5 before performing ultrasound measurements. The TF_{di} measurement was carried out at the level of the Zone of Apposition (ZOA) of the right and left hemidiaphragm along the midaxillary line (Figures 1,2).

A linear high-frequency probe (13 - 6 MHz) is placed along the mid-axillary line. The zone of apposition of the diaphragm with the chest wall is located caudal to the costodiaphragmatic recess. A good acoustic window is found between two ribs, and a 2D clip is acquired while the patient is asked to perform a maximal inspiratory effort, starting from functional residual capacity. The thickness of the diaphragm is measured at end-expiration (T_{EE}) and peak-inspiration

Figure 1: Probe placement to explore the diaphragm in the Zone of Apposition (ZOA).

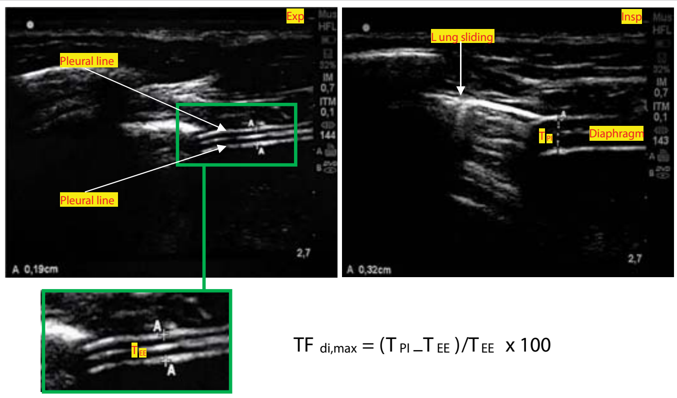

Figure 2: Method of measuring the diaphragm thickness fraction.
TEE: Thickness at end-expiration. TPI: Thickness at end peak inspiration.
TFdi,max = (TPI–TEE) / TEE x 100

(T_{PI}). $TF_{di,max}$ is calculated with the following formula: $TF_{di,max} = (T_{PI} - T_{EE})/T_{EE}$. $TF_{di,max}$ = maximal diaphragmatic thickness fraction during inspiration [36-39].

The TF_{di} was calculated at the time of data analysis using the following formula: $TF_{di,max} = (T_{PI} - T_{EE})/T_{EE}$ [9]. TF_{di} was calculated for each hemidiaphragm, then an average value was assigned for each patient, which was used to reflect the overall diaphragmatic function. The treating team was not notified of the results of the examination.

Covariates

For each patient, we evaluated their age, gender, weight, height, body mass index (BMI), nutritional status, smoking, comorbidities, ASA Physical Status Classification [34], estimated functional capacity in metabolic equivalents (METs) was estimated from standard published tables based on protocol and total time completed in the final stage [35]. Also, we collected some biological data such as preoperative kalemia and albuminemia and pre and post-operative hemoglobin. We also collected information related to surgical and anesthetic procedures.

Anesthetic Procedure

The anesthesia protocol systematically included anesthesia balanced by propofol associated with fentanyl and non-depolarizing curare (rocuronium or cis-atracurium). Etomidate was proposed for patients with precarious hemodynamic conditions. The monitoring of the neuromuscular block was carried out by the analysis of the «train of four» at the adductor of the thumb. Locoregional analgesia by an epidural catheter or Rachianalgesia with morphine 0.2 mg was performed as much as possible. Multimodal analgesia included Paracetamol (except in cirrhotic patients) and morphine according to VAS was started postoperatively. Recourse to a morphine PCA could be proposed as soon as the patient was admitted to ICU. Extubation was carried out as early as possible. Decurarization was carried out systematically. The indication of post-operative supervision in the ICU was foreseen from the pre-operative period and depended on the patient's history and the type of surgery.

Outcomes

The principal endpoint of the study was the development of PPCs. This was a composite parameter defined by the occurrence of pneumonia, atelectasis, hypoxemia ($PaO_2 < 60$ mmHg), respiratory acidosis (pH < 7.38), pleural effusion, rescues to non-invasive ventilation (NIV), reintubation, or the need for prolonged mechanical ventilation in the postoperative period. The patient's medical record was reviewed to determine if the diagnosis of PPCs was made by the treating team. Clinicians were not aware of any of the measured parameters in the study.

Definitions

Pneumonia was defined according to the Centers for Disease Control definition [40]. Atelectasis was defined as a new postoperative lung consolidation in the absence of pneumonia criteria on a chest x-ray. Hypoxemia and respiratory acidosis were defined by measurement of $PaO_2 < 60$ mmHg and pH < 7.38 respectively. The diagnosis of pleural effusion was made by standard radiography or pleuropulmonary ultrasound. Mechanical ventilation was defined as prolonged if it lasted more than 24 hours after the operation, as defined by the Society of Thoracic Surgeons (STS) [41].

Statistical analyses

Data are presented as the mean ± standard deviation for variables with a normal distribution and as the median and interquartile range for variables with skewed distribution. Categorical variables were presented as counts and percentages. Parametric or nonparametric tests were used for continuous variables as appropriate after the normality of the distribution was tested by the Kolmogorov-Smirnov test. Group comparisons of continuous variables were made using the Student t-test or Mann-Whitney U test, as appropriate. For the categorical variables, group comparisons used the chi-2 test or the exact Fischer test. Analysis of variance (ANOVA) for repeated measures was used to compare continuous variables over time. Bonferroni's post hoc test was used to locate the significance. Receiver operating characteristic curves and the respective areas under the curves (AIC) were calculated for $TF_{di,max}$. The best cutoff value was chosen using Youden's index. The sensitivity, specificity, and positive and negative likelihood ratios (LH) (with 95% confidence intervals (95%CI)) were calculated at the best cutoff value. This value was used to divide patients into two categories. Univariate and multiple logistic regressions were performed to identify factors potentially associated with the occurrence of PPCs. Variables with a value of $p < 0.1$ in univariate analyses were introduced to the multiple models. Other variables known in the PPCs literature were forced into the multiple models. Results are presented as the odds ratio (OR) and 95%CI. A two-tailed p value < 0.05 was considered significant. Assuming a 30% occurrence of PPC [42], a sample size of 160 patients was required to detect an OR 2.5 for a low $TF_{di,max}$ with 80% power and a two-sided alpha of 0.05. The analyses were conducted with IBM SPSS Statistics (IBM Corp, Armonk, NY, USA).

Ethical considerations

The study was carried out in accordance with the Helsinki Declaration. Our protocol was approved by the Committee on Ethics for Biomedical Research of the Faculty of Medicine and Pharmacy of Rabat. Free and informed consent was obtained.

Results

Patient characteristics

During the study period, 238 patients were admitted to

ICU. 180 patients were recruited, of which 159 were included for analysis. 21 patients were excluded after registration for problems with the management of the surgical program or because of the unavailability of labile blood products on the day of surgery (Figure 3). Demographic and clinical characteristics of the study are shown in Table 1. The age of the study population was 55.5 ± 8.1 years, and 52.8% were male. In our study, ICU mortality was 7.5% (12 patients died).

Postoperative pulmonary complications

Overall, 55 patients (34.6%) developed the composite PPCs result. 28 patients developed atelectasis (17.6%), 27 patients (17%) used NIV postoperatively, hypoxemia was found in 24 patients (15.1%), 10 patients were reintubated (6.3%) and 8 patients developed pneumonia (5%) (Table 2).

Patients with PPCs were more undernourished [7 (6.7) *vs.* 10 (18.2); $p = 0.026$], and had a lower pre-operative hemoglobin [11.6 ± 1.37 *vs.* 12.37 ± 1.45; $p = 0.001$]. In terms of anesthetic and surgical techniques, supramesocolic surgery was more often complicated by PPCs [29 (52.7) *vs.* 26 (47.3); $p < 0.001$], whereas epidural patients developed

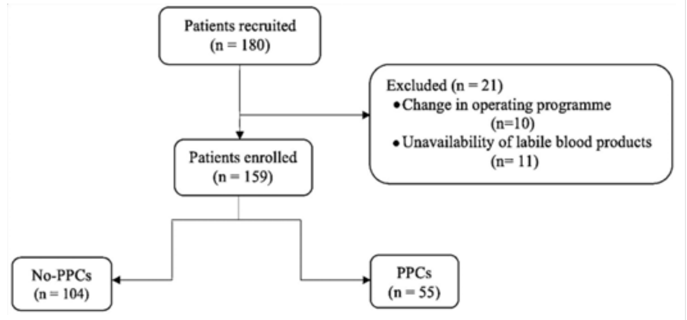

Figure 3: Study flow chart.

Table 1: Sample characteristics.

Parameter	Total (*n* = 159)	No-PPCs (*n* = 104)	PPCs (*n* = 55)	*p* - value
Age (years)[a]	55.5 ± 8.16	54.98 ± 9.21	56.71 ± 5.57	0.14
Gender (n (%))				1
Men	84 (52.8)	55 (52.9)	29 (52.7)	
Women	75 (47.2)	49 (47.1)	26 (47.3)	
Weight (kg)[a]	63.21 ± 8.80	62.82 ± 8.54	64 ± 9.31	0.43
Cut (m)[a]	1.64 ± 0.04	1.64 ± 0.04	1.64 ± 0.04	0.73
BMI (Kg/m^2)[a]	23.6 ± 3.94	23.40 ± 3.88	23.9 ± 4.07	0.45
Undernutrition (n (%))	17 (10.7)	7 (6.7)	10 (18.2)	0.026
OSAS (n (%))	16 (10.1)	12 (11.5)	4 (7.3)	0.39
ASA (n (%))				0.16
I	77 (48.4)	49 (47.1)	28 (50.9)	
II	67 (42.1)	48 (46.2)	19 (34.5)	
III	15 (6.9)	7 (6.7)	8 (14.5)	
Functional capacity (n (%))				0.067
> 4MET	116 (73)	71 (68.3)	45 (81.8)	
< 4MET	43 (27)	33 (31.7)	10 (18.2)	
Smoking (n (%))				0.54
Non-smoker	98 (61.6)	62 (59.6)	36 (65.5)	
Ex-smoker	37 (23.3)	27 (26)	10 (18.2)	
Smoker	24 (15.1)	15 (14.4)	9 (16.4)	
COPD (n (%))	10 (6.3)	7 (6.7)	3 (5.5)	0.96
Heart disease (n (%))	22 (13.8)	14 (13.5)	8 (14.5)	0.85
CRF (n (%))	4 (2.5)	2(1.9)	2(3.6)	0.60
Arterial hypertension (n (%))	53 (33.3)	34 (32.7)	19 (34.5)	0.81
Diabetes (n (%))	42 (26.4)	28 (26.9)	14 (25.5)	0.84
Preoperative Hb (g/dl)[a]	12.10 ± 1.46	12.37 ± 1.45	11.6 ± 1.37	0.001
Postoperative Hb (g/dl)[a]	10.68 ± 1.24	10.81 ± 1.25	10.44 ± 1.21	0.07
Kalemia (mmol/L)[a]	4.2 ± 0.62	4.17 ± 0.61	4.25 ± 0.64	0.44
Albuminemia (g/L)	32.36 ± 3.14	32.70 ± 3.18	31.73 ± 2.99	0.06
Type of surgery (n (%))				<0.001
Upper abdominal surgery	48 (30.2)	19 (18,3)	29 (52.7)	
Submesocolic	111 (69.8)	85 (81.7)	26 (47.3)	
Laparoscopy (n (%))	83 (52.2)	57 (54.8)	26 (47.3)	0.36
Surgical duration (hours)[a]	4.49 ± 0.87	4.42 ± 0.80	4.62 ± 0.98	0.17
Intraoperative transfusion (n (%))	20 (12.6)	14 (13.5)	6 (10.9)	0.64
Epidural analgesia (n (%))	27 (17)	23 (22.1)	4(7.3)	0.018
Rachianalgesia (n (%))	88 (55.3)	62 (59.6)	26 (47.3)	0.13
Postoperative morphine (n (%))	115 (72.3)	71 (68.3)	44 (80)	0.11
Extubation delay (min)[b]	90 (60-120)	90 (45-90)	90 (60-120)	0.37
LOS in ICU (days)[b]	4 (1-7)	1 (1-5)	7 (6-9)	<0.001
ICU mortality (n (%))	12 (7.5)	4 (3.8)	8 (14.5)	0.024

[a] expressed as mean ± standard deviation, [b] expressed as median (interquartile range). BMI: Body Mass Index; OSAS: Obstructive Sleep Apnea Syndrome; ASA: American Society of Anesthesiologists; MET: Metabolic Equivalent; COPD: Chronic Obstructive Pulmonary Disease; CRF: Chronic Respiratory Failure; Hb: Hemoglobin; LOS: Length of Sta;, ICU: Intensive Care Unit.

Table 2: Comparison of occurrence of PPCs depending on survivors and the dead.

Variables (*n* (%))	Total (*n* =159)	Survivors (*n* =147)	Dead (*n* = 12)	*p* - value
Atelectasis	28 (17.6)	25 (17)	3 (25)	0.44
Hypoxemia	24 (15.1)	19 (12.9)	5 (41.7)	0.020
Pneumonia	8 (5)	3 (2)	5 (41.7)	<0.001
Respiratory acidosis	7 (4.4)	6 (4.1)	1 (8.3)	0.42
Recourse to the NIV	27 (17)	26 (17.7)	1 (8.3)	0.69
Use of oxygen	36 (22.6)	30 (20.4)	6 (50)	0.029
Pleural effusion	5 (3.1)	4 (2.7)	1 (8.3)	0.32
Extubation failure	10 (6.3)	6 (4.1)	4 (33.3)	0.003
PPCs (composite)	55 (34.6)	47 (32)	8 (66.9)	0.024

Expressed in effective (percentage). NIV: Non-Invasive Ventilation; PPCs: Post-operative Pulmonary Complications.

significantly fewer PPCs [23 (22.1) *vs.* 4(7.3); $p = 0.018$]. The length of ICU stays was significantly longer in patients with PPCs [4 (1-7) *vs.* 1 (1-5) days, $p < 0.001$]. In terms of mortality, it was significantly higher in the PPCs group [4 (3.8) *vs.* 8 (14.5); $p = 0.024$].

Diaphragmatic ultrasound

Regarding the analysis of ultrasound data, the mean $TF_{di,max}$ was 40.23% ± 12.02, It was significantly less in patients with PPCs [44.83% ± 11.07 *vs.* 31.54% ± 8.45; $p < 0.001$] (Table 3). Its value decreased significantly on day 1 and day 3 compared to its preoperative value (Figure 4). The postoperative change in $TF_{di,max}$ observed in our study was significantly greater in patients without PPCs [-15.2% (-22, -9) *vs.* -6.5% (-9.5, -4.5) $p < 0.001$] (Figure 5).

Predictive value of diaphragmatic thickness fraction

The performance of diaphragmatic ultrasound to predict a patient at risk of PPCs is summarized in Table 4 and the ROC curve is shown in Figure 6. The best predictor was the presence of a preoperative $TF_{di,max}$ < 37% [Sensitivity: 72.7%, 95% IC: 59.0 – 83.8; Specificity: 80.8, 95% IC: 71.8 – 87.8; PPV: 66.6%; NVP: 84.8%; AIC: 0.832, 95% IC: 0.754 – 0.887]. Positive and negative Likelihood Ratio were respectively 3.7 (95% IC: 2.4 – 5.7) and 0.3 (95% IC:0.2 – 0.5), which is a moderate value of discrimination between the PPCs and no-PPCs group.

Diaphragmatic thickness fraction predictors of PPCs

In multiple logistic regression, the $TF_{di,max}$ was included in the regression model. $TF_{di,max}$ < 37% [OR: 7.10; 95% CI: 1.71 – 18.60; $p < 0.001$] and supramesocolic surgery [OR: 9.94; 95%CI: 3.62 – 27.29; $p < 0.001$] were independently related to the occurrence of PPCs. However, performing an epidural was a protective factor [OR: 0.21; 95% CI: 0.052 – 0.87; $p = 0.031$] (Table 5).

Discussion

In our prospective cohort of digestive cancer curative surgery, 55 patients (34.6%) of the 159 included in the study developed PPCs. Supramesocolic surgery was the main risk factor associated with their occurrence. However, the introduction of epidural analgesia was a protective factor.

Table 3: Ultrasound data.

Parameter	Total (*n* = 159)	No-PPCs (*n* = 104)	PPCs (*n* = 55)	*p* - value
$TF_{di,max}$ preoperative(%)[a]	40.23 ± 12.02	44.83 ± 11.07	31.54 ± 8.45	<0.001
$TF_{di,\ max}$ day (%)[a]	27.34 ± 7.34	29.31 ± 7.63	23.61 ± 4.98	<0.001
$TF_{di,\ max}$ day 3(%)[a]	26.46 ± 5.19	28.61 ± 3.98	24.59 ± 5.43	<0.001
Change of $TF_{di,max}$ at day 1(%)[b]	-10 (-21,-6,5)	-15.2 (-22, -9)	-6.5 (-9.5, -4.5)	<0.001
Change of $TF_{di,max}$ at day 3 (%)[b]	-5 (-6,5, -3)	-5 (-6.5, -3.2)	-3.5 (-6, -2.5)	0.017

[a] expressed as mean standard deviation, [b] expressed as median (interquartile interval), $TF_{di,max}$: maximum diaphragm thickness fraction.

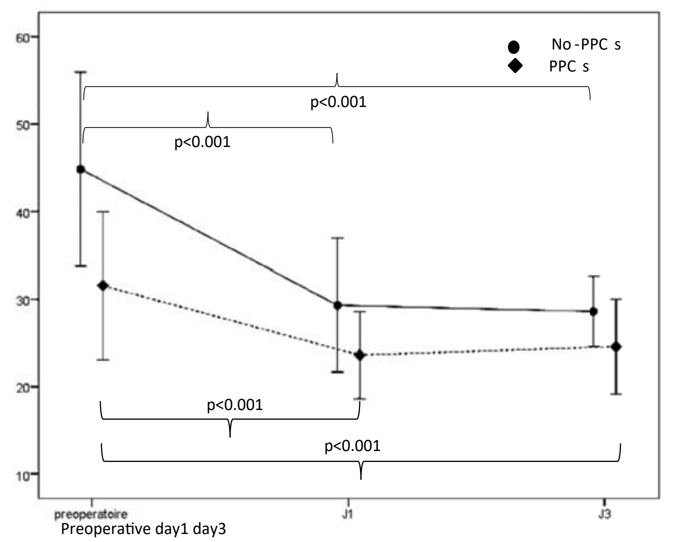

Figure 4: Evolution of $TF_{di,max}$ between its preoperative value, day 1 and day 3.

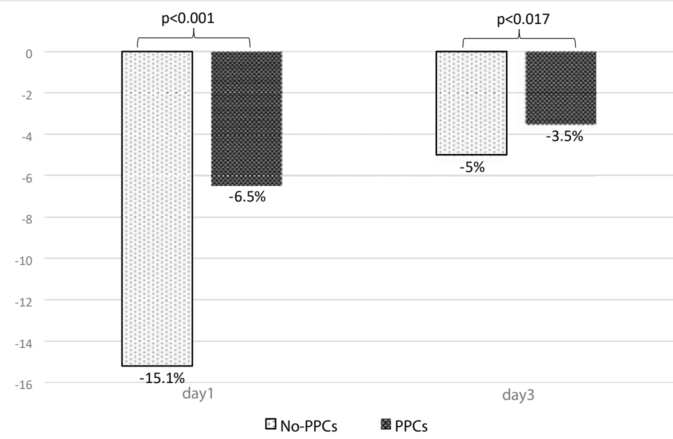

Figure 5: Change in $TF_{di,max}$ between preoperative and day1, preoperative and day 3.

Table 4: Diaphragmatic ultrasound performance to predict the risk of PPCs occurring at a $TF_{di.}$

Cutoff value: TF_{di} = 37%	Values	95%IC
Sensitivity	72.7%	59.0 – 83.8
Specificity	80.8%	71.8 – 87.8
Positive Likelihood Ratio	3.7	2.4 – 5.7
Negative Likelihood Ratio	0.3	0.2 – 0.5
Prevalence of the disease	34.5%	27.2 – 42.5
Positive Predictive Value (PPV)	66.6%	56.6 – 75.3
Negative predictive value (NPV)	84.8%	78.2 – 89.7
Accuracy	77.9%	70.7 – 84.1

Table 5: Preoperative risk factors of PPCs.

Variable	Univariate analysis			Multivariate analysis		
	OR	95%IC	*p*	OR	95%IC	*p*
Age	1.02	0.98 – 1.07	0.20	1.01	0.94 – 1.07	0.76
BMI	1.03	0.95 – 1.12	0.44	–	–	–
Undernutrition	3.08	1.10 – 8.61	0.032	1.01	0.94 – 1.07	0.75
ASA				–	–	–
I	1					
II	0.69	0.34 – 1.40	0.30			
III	2	0.65 – 6.10	0.22			
Smoking				–	–	–
Non-smoker	1					
Ex-smoker	0.63	0.27 – 1.46	0.94			
Smoker	1.03	0.41 – 2.6	0.29			
COPD	1.25	0.31 – 5.04	0.75	–	–	–
Functional capacity				–	–	–
> 4MET	1					
< 4MET	2.09	0.94 – 4.65	0.15			
Preoperative Hb	0.67	0.52 – 0.86	0.002	0.84	0.61 – 1.16	0.29
Epidural	0.018	0.10 – 0.95	0.041	0.21	0.052 – 0.87	0.031
Type of surgery						
Submesocolic	1					
Upper abdominal surgery	5	2.41 – 10.31	<0.001	9.94	3.62 – 27.29	<0.001
TFdi,max <37%	8	3.81 – 16.78	<0.001	7.10	1.71 – 18.60	<0.001

BMI: Body Mass Inde; ASA: American Society of Anesthesiologists; MET: Metabolic Equivalen; COPD: Chronic Obstructive Pulmonary Diseas; Hb: Hemoglobi; $TF_{di,max}$: maximum diaphragm thickness fraction

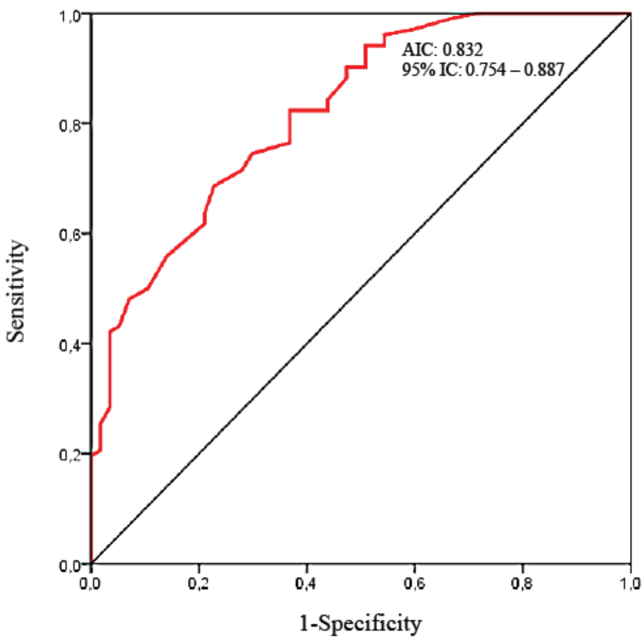

Figure 6: Receiver Operating Curve (ROC) of preoperative $TF_{di,max}$ for discrimination of No-PPCs and PPCs groups after digestive cancer curative surgery.

The analysis of the ROC curve showed that a pre-operative $TF_{di,max}$ of less than 37% was associated with the occurrence of PPCs with a sensitivity of 72.7% and a specificity of 80.8%. $TF_{di,max}$ decreased postoperatively and remained lower in patients with PPCs. In terms of "outcome", the length of stay in the ICU was significantly longer in patients who developed PPCs with significantly more deaths.

PPCs are as common as cardiovascular complications. Their incidence varies greatly in the literature. This is due to the multiple definitions that have been used. Moreover, few studies have studied the occurrence of these PPCs in a homogeneous population taking into account the surgical technique, the path first, the existence of an induction treatment, and so on. However, the percentage between 10% and 25% according to the series [43-46] seems to be currently falling. In general, and according to standardized definitions, the rate of pulmonary complications is 39% and they account for nearly 60% of hospital deaths. In our cohort, the PPCs rate was around 34.6%, with significantly higher mortality.

The factors favoring the occurrence of PPCs are multiple [43-53]. Some are linked to the patient (poor pre-operative ventilator performance, smoking, nutritional status, induction treatment). Others are related to the intervention (duration of the operation, mechanical ventilation, transthoracic surgical approach). Finally, the postoperative period, in particular the management of pain and fluid intake, also seems to be involved in the genesis of these complications. The site of the incision is an important predictor of PPCs. The ventilatory impact of supraumbilical digestive surgery is a risk factor regardless of patient history. The risk decreases when the incision moves away from the diaphragm [54-56].

Our results corroborate this effect, in our multiple regression model, upper abdominal surgery was identified as a risk factor independently related to the occurrence of PPCs [OR: 9.94; 95% CI: 3.62 – 27.29; *p* < 0.001].

These «macro-events» probably mask the protective influence that can have some practices, perfectly known from high volume centers: protocolized management of perfused volumes in intraoperative, early extubation, choice of epidural analgesia for the postoperative period, noninvasive ventilation...

The thoracic epidural analgesia has several theoretical elements suggesting a decrease in pulmonary complications of heavy surgery, especially major abdominal ones. A complete and didactic review of the literature has been published [57]. Epidural analgesia with local anesthetics alone or, better, in combination with opiates, appears to be more effective on pain than parenteral opioid analgesia, including self-administered administration. Therefore, it should promote coughing and early postoperative mobilization. In addition, by blocking the inhibitory reflexes of diaphragmatic function seen in abdominal surgery, epidural analgesia with local anesthetics is expected to improve diaphragmatic dysfunction. Evidence of a beneficial effect on gastric graft vitality and PPCs has recently been provided [58]. Again, our study showed that the use of an epidural for postoperative analgesia was associated with a reduction in PPCs [OR: 0.21; 95% CI: 0.052 – 0.87; $p = 0.031$].

A relative weakness of the diaphragm was very common in the patients included in the study. The mean value of TF_{di} in healthy subjects is approximately 80% - 100% with the 5th percentile of 20% - 30% [59]. In comparison, the pre-operative TF_{di} mean for patients in our study was 40% or half of normal. One in four patients had TF_{di} below the fifth percentile of normal. Several factors may explain why the preoperative diaphragmatic contractile reserve of our patients is altered. The neoplastic context of our population explains part of this result [60,61]. The current treatment of digestive cancers is part of multidisciplinary management based on neoadjuvant Radio-Chemotherapy (RCT). Nearly 50% of patients undergoing surgery are currently benefiting from this strategy. The presence of induction therapy is considered by some teams [43,57,58] as a factor of hospital excess mortality but the controversy continues as many studies have not found an obvious relationship between the occurrence of PPCs and RCT [62]. Radiation therapy, depending on the doses administered, adds the possibility of lung or pleural parenchymal involvement and promotes surgical complications. The PPCs rates depend closely on the volume of irradiation. The higher the dose of radiation therapy, the greater the incidence and severity of PPCs. The same applies to the diffusion capacities of the alveolar-capillary membrane [62]. Chemotherapy participates in general immunosuppression and promotes postoperative infectious events. As a result, unexpected bacterial or viral agents were identified on postoperative lung biopsies, particularly after RCT [63].

In addition, cancer and chemotherapy are major risk factors for undernutrition. In our cohort, the presence of preoperative undernutrition was significantly associated with the occurrence of PPCs [OR: 3.08; 95% CI: 1.10 – 8.61; $p = 0.32$]. Undernourished patients with or without chronic obstructive pulmonary disease have atrophy of the accessory respiratory muscles and diaphragm [64] with decreased maximum ventilation per minute [65]. Malnutrition also leads to decreased ventilatory responses to hypoxia and hypercapnia. The occurrence of atelectasis is theoretically favored by undernutrition. Indeed, it is experimentally demonstrated that undernutrition decreases surfactant synthesis. On the other hand, there is a decrease in the frequency of sighs and a decrease in the strength of the expiratory muscles [65]. The increased risk of infection, particularly in the lung of undernourished patients, is a classic notion. The occurrence of pneumopathy following digestive surgery is more common in patients with preoperative protein malnutrition.

Decreased diaphragmatic function in postoperative is almost constant after major abdominal surgery. The occurrence of PPCs is the combination of deleterious effects of anesthesia, mechanical ventilation, and surgery on respiratory function. General anesthesia modifies ventilation/perfusion ratios, as well as the value of chest volumes and compliances. This results from the combination of supine position and muscle relaxation. It is the consequence of ventilatory disorders or atelectasis present mainly in declivized areas. These phenomena are exacerbated by a diaphragmatic dysfunction related to a reflex inhibition of phrenic innervation, presumably not related to pain since the administration of morphine by the epidural route does not improve the diaphragmatic function. Only the use of local anesthetics as part of epidural analgesia can lead to an improvement in diaphragmatic dysfunction, which however remains only partial [66]. Diaphragmatic atony will persist for several hours or even several days, either by neurogenic reaction or by direct trauma related to surgery (stretching, compression, phrenotomy). These combined factors constitute a restrictive syndrome that persists for more than two weeks but is particularly important during the first seven days. All these elements are added to the digestive distension relative to the postoperative ileus to reduce the effectiveness of the cough.

In addition, the adverse effects of mechanical ventilation have been incriminated in recent years in the genesis of PPCs. It has been shown that a few hours of fully controlled mechanical ventilation leads quickly to atrophy and a decrease in contractility strength both in vivo and in vitro [67-70]. Indeed, it seems that mechanical ventilation is capable of producing per se complications of mechanical, hydrostatic, and inflammatory origin called «lesions induced by mechanical ventilation» (Ventilator-Induced Lung Injury VILI) [71]. These lesions are attributed to barotrauma, volotrauma, and more recently biotrauma. These inflammatory phenomena could also continue with the maintenance of postoperative ventilation. The current recommendations recommend that the postoperative ventilation time be shortened to a minimum and that anesthetic protocols be used to allow for rapid extubation of the "fast track recovery" type [47,72]. Finally, some insist on the need for intraoperative corticosteroids to reduce the occurrence of inflammatory phenomena. However, the results of such practices remain insufficient to propose them systematically [73,74].

The ventilatory effects of upper abdominal surgery are mainly due to a decrease in diaphragmatic inspiratory function. This diaphragmatic dysfunction may be responsible for a 30% - 40% decrease in lung volumes in upper abdominal surgery [75]. These abnormalities are maximum on the first postoperative day but usually persist for two weeks [75]. This alteration of contractile function is multifactorial: surgical aggression, inflammatory reaction, anesthetic agents, and postoperative pain [76]. The mechanical aggression represented by parietal muscular decay during surgery is one of the main factors at the origin of postoperative diaphragmatic muscular dysfunction. However, the importance of parietal decay (and especially abdominal muscle sections) is not sufficient to explain the occurrence of diaphragmatic dysfunction, as it is also observed after laparoscopic surgery [77]. One of the main mechanisms of diaphragmatic dysfunction could be a reflex inhibition of the phrenic inspiratory discharge, the starting point of which would be at the level of the visceral afferences of the mesenteric region [78].

However, the postoperative change in TF_{di} observed in our study was significantly greater in patients without PPCs, this can be explained by a higher preoperative value of $TF_{di,max}$ in patients without PPCs. Thus, it would appear that the preoperative $TF_{di,max}$ value is the main predictor of PPCs occurrence. A low preoperative $TF_{di,max}$ helped to predict the occurrence of CCPs after digestive cancer curative surgery. In contrast with previously described risk factors, diaphragm function could be improved with inspiratory muscle training with potentially positive impacts on outcomes.

Our cohort identified and described a simple, easy, and affordable means of inspirational muscle weakness that could help identify vulnerable patients who could benefit from preventive strategies. To our knowledge, no study has yet highlighted the contribution of diaphragmatic ultrasound in digestive cancer curative surgery to assess the risk of PPCs. However, our work has its limits. Our study did not analyze the impact of fragility and sarcopenia indicators in the genesis of PPCs. Also, skin marking was not used, making it possible to compare repeated measurements in the same patient at different times. Finally, Postoperative TF_{di} measurements may have been affected by a decrease in inspiratory effort in the context of postoperative pain despite resorting to a multimodal postoperative analgesia strategy.

However, despite a moderate discrimination value reflected by LR, it seems that the association between a $TF_{di,max}$ less than 37%, and the occurrence of PPCs is strong. It is important to note that none of the limitations mentioned should have affected the relationship between preoperative mean $TF_{di,max}$, and the incidence of PPCs, which was our main analysis.

Conclusion

In this prospective cohort study conducted in adults undergoing digestive cancer curative surgery, we have demonstrated that a maximum average thickness fraction of less than 37% is a major predictor of PPCs, with a sensitivity of 72.7% and specificity of 80.8%. TF_{di} decreased significantly in the postoperative period and remained lower in patients with pulmonary complications. This easily accessible marker of diaphragmatic weakness could, therefore, help identify vulnerable patients who would benefit most from preventive strategies such as preoperative training of the inspiratory muscles. However, the 37% threshold value calculated in this preliminary study will need to be validated in future clinical studies that include a significant number of patients before it can be proposed for clinical practice.

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Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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