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Research Article

I-BREATHE: An Epidemiological Study in Gynaecology-Oncology Surgeries

Viktor Cassar[1], Tim Langdon[2], Ioanna Antoniou[1], James Watkin[2], Porfyrios Korompelis[1], Christine Ang[1], Andrew Bracewell[2], Bhaskar Dutta[2*]

[1]Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, Gateshead, United Kingdom; [2]Department of Anaesthesiology, Queen Elizabeth Hospital, Gateshead, United Kingdom

ABSTRACT

Background: Chest infections and other Postoperative Pulmonary Complications (PPC) are a major cause of morbidity and prolonged hospital stay following major abdominal surgery. The incidence of PPC could be as high as 20% for upper abdominal surgeries, however this is not well studied amongst patients undergoing surgery for gynaecological cancer.

Methodology: This is a single centre epidemiological study in a large tertiary gynaecological oncology centre, the Northern Gynaecological Oncology Centre (NGOC), United Kingdom. A preventing PPC Working Group was developed and a peri-operative respiratory optimisation pathway called the I-BREATHE was introduced in October 2021. In our analysis, patients who underwent a major laparotomy in 2019 (group A) prior the introduction of the intervention were captured retrospectively, whilst patients who underwent a major laparotomy between October 2021 to October 2022 (group B) were captured prospectively. The study compared the absolute incidence of postoperative chest infection, mortality and in-hospital length of stay.

Results: The study included a total of 394 patients; 237 patients were included in group A and 157 patients were included in group B. The incidence of chest infection was 15.2% in group A and 15.3% in group B (Relative Risk (RR) 1, 95%, Cumulative Incidence (CI) 0.63-1.62, p=0.98). A sub-group analysis demonstrated a significant decrease in the incidence of chest infections in smokers and ex-smokers, with reduction in incidence from 27.6% (group A) to 7.1% (group B) (RR: 0.26, 95% CI 0.065-1.032, p=0.03). There was a significant reduction in the total in-patient hospital stay and ward-based length of stay by a median of 2-days in group B compared to group A.

Conclusion: The addition of a structured peri-operative respiratory care optimisation bundle within the Enhanced Recovery After Surgery (ERAS) protocol in high-risk patients having surgery for gynaecological malignancy has been seen to be very effective in the cohort of patients with a history of smoking, with a significant reduction in the incidence of chest infections. Moreover, the implementation of these strategies has shown a significant reduction in in-patient length of stay. In view of the limitations of the study more research is needed to definitively recommend our initiative to all types of high-risk surgeries.

Keywords: Postoperative Pulmonary Complications (PPC); Enhanced Recovery After Surgery (ERAS); Gynaecological oncology surgery

INTRODUCTION

Chest infections and other pulmonary complications can be significant consequences of surgery, constituting to a large proportion of morbidity and mortality following major abdominal surgery. It is estimated that the incidence of Postoperative Pulmonary Complications (PPC) could range from 0–5% for lower abdominal and 16–20% for upper abdominal surgeries [1].

There are a multitude of factors affecting the incidence of PPC, which can be largely grouped as patient associated and operative associated factors. Patient associated factors include age over 65 years, American Society of Anaesthesiologist's (ASA) physical status score of more than 2, history of pulmonary disease, presence of malignancy and smoking status at the time of surgery. Operative risk factors include, the nature and complexity of the surgery, the type of incision, operative time over 2.5-hours, blood

Correspondence to: Bhaskar Dutta, Department of Anaesthesiology, Queen Elizabeth Hospital, Gateshead, United Kingdom, Tel: +44-191-4456476; E-mail: bdutta@nhs.net

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loss of more than 500 ml, blood transfusion and insertion of a nasogastric tube in the peri-operative period [2].

Gynaecological cancers primarily involve four cancer sites-vulva, cervix, uterus and ovary. The pathogeneses around the various tumour sites vary considerably, affect distinctly separate population cohorts and are managed very differently. Patients undergoing radical surgery in gynaecological cancers have been seen to have higher incidence of PPCs among other post-operative morbidities [3-5]. Post-operative morbidity and PPC in this high-risk group of patients can significantly hinder their cancer treatment journey, amounting to a possible delay in receiving adjuvant treatment, which may impact treatment outcomes. There are other consequences of these complications including prolonged in-patient stay, re-admission to the high dependency or intensive care unit during an index admission or re-admission to the hospital following discharge, all resulting in poorer patient outcomes and an increased cost to the healthcare system [6].

There is an evidence in the literature that Enhanced Recovery After Surgery (ERAS) pathways, especially those incorporating a dedicated respiratory optimisation bundle reduce the incidence of PPCs [7]. But impact of such a bundle has never been studied in gynaecological oncology surgeries. In view of this, we started a project at the Northern Gynaecological Oncology Centre (NGOC), Gateshead, United Kingdom (UK), to determine the incidence of chest infections in major gynaecology-oncology surgeries, followed by establishing a holistic respiratory optimisation pathway integrated within the perioperative ERAS protocol, looking at optimising the perioperative care of these patients and prospectively analysing the effectiveness of the pathway. The aims (primary outcomes) of this project were to assess whether respiratory optimisation interventions reduce the incidence of chest infections, mortality after surgery and in-patient hospital stay.

METHODOLOGY

Retrospective study: 2019

In order to describe specific interventions and formulate an effective peri-operative respiratory optimisation pathway it was most important to establish the baseline incidence of post-operative chest infection within the cohort of patients with gynaecological cancers undergoing a major open abdominal surgery. Moreover, we aimed to identify modifiable risk factors within this group of patients and determine the association of post-operative length-of-stay and mortality in the context of post-operative chest infections. It was decided that the best way to assess these factors was to perform a single-centre retrospective study.

All patients who underwent a laparotomy and major abdominal surgeries at the NGOC between January 2019 and December 2019 were included in the study. The patients were identified using the electronic surgical-listing records and these were cross-referenced with electronic operation notes and discharge letters. Included cases were assessed and demographic, pre-operative American Society of Anaesthesiologist's (ASA) physical status, post-operative morbidity data, in-patient hospital stay and survival data were recorded. The identification of post-operative chest infection was established if there was a clear diagnosis on ward or critical care discharge letters and/or radiology report of pneumonic changes with antibiotic treatment for chest infections, in line with the European Perioperative Clinical Outcome (EPCO) definitions [8]. The extent of surgery was assessed using a surgical complexity score and patients were further stratified into three groups, they are low, intermediate or high surgical complexity, to allow for further analysis [9].

Development of the I-BREATHE pathway

A Preventing PPC Working Group was developed. After reviewing the literature, it was decided to design a programme, which revolves around engaging patients and their close family members, helping them to choose healthy lifestyle choices. Specific interventions were delineated at different points during the patient's peri-operative journey. We made sure that the pathway includes measures in accordance with the 2021 perioperative guideline of the preoperative association, United Kingdom (UK), to make this programme global and applicable to the recent standards [10].

The acronym I-BREATHE was designed for summarising the different components of the programme and for ease of recall amongst staff and patients.

- I-Incentive spirometry
- B-Brushing teeth and using mouthwash twice daily
- R-Raise head of bed
- E-Exercise and mobilise (moderate intensity exercise 20-25 mins/day)
- A-Ask questions (benefits, risks, alternatives, do nothing)
- T-Take deep breaths and cough
- H-Healthy life-style (stop smoking, reduce alcohol and eat healthy)
- E-Engage (patient and family education)

A 6-minute patient information video describing the different components of I-BREATHE and their importance was developed using representatives from the hospital's Acute Response Team and the physiotherapy department.

Prospective study: 2021-2022

The preventing PPC working group appointed representatives to organise training on I-BREATHE and the different interventions, for all stakeholders involved including the various teams in the pre-assessment unit, theatres, Intensive-Care Unit (ICU), and the post-operative wards between July 2021 and September 2021. The full project was funded by the Trust's Surgical Business Unit (SBU) and was rolled out in October 2021.. The prospective study spanned over 12-months.

The preoperative interventions of the study was comprehensive. Patients were shown the I-BREATHE video during their pre-assessment appointment on a standard handheld electronic device. Every patient was provided with an incentive spirometer to facilitate breathing exercises at home preoperatively and was asked to perform 8-10 breaths four times a day. Patients received one-to-one training on how to perform these exercises by the preassessment nurses and were advised to bring the spirometer to the hospital on the day of their admission, so that the exercises can be continued postoperatively. Patients were also provided with chlorhexidine mouthwash to be used in the peri-operative period; and prophylactic mucolytic (carbocisteine 375 mg, three times daily) was prescribed to patients with history of smoking, COPD and bronchiectasis, in the absence of any contraindication. Preoperative smoking cessation interventions were taken. Patients were also advised exercises based on UK (United Kingdom) Chief Medical Officers' Physical Activity Guideline to improve their aerobic capacity [11]. This included advice to do moderate intensity exercises, for example brisk walking, cycling or swimming for 150 minutes per week (20-25 minutes per day) or high intensity exercises for 75 minutes per week, whichever was feasible.

Patients underwent a Cardio-Pulmonary Exercise Test (CPET), unless they were unable to do the exercise; and their perioperative risks were explained based on the American College of Surgeons (ACS) National Surgical Quality Improvement Programme (NSQIP) risk scoring tool [12].

In the postoperative period, with the help of the physiotherapy team, early patient mobilisation and lung expansion exercises were encouraged. In order to improve compliance and act as an aide-memoire, a standardised prescription bundle was created (Figure 1), on the electronic medication prescribing system, so that nursing team could document strict adherence to all the I-BREATHE measures. The elements of this prescription included incentive spirometry 4-times a day, twice daily use of mouthwash, twice-daily teeth brushing, twice-daily mobilisation and carbocisteine as required.

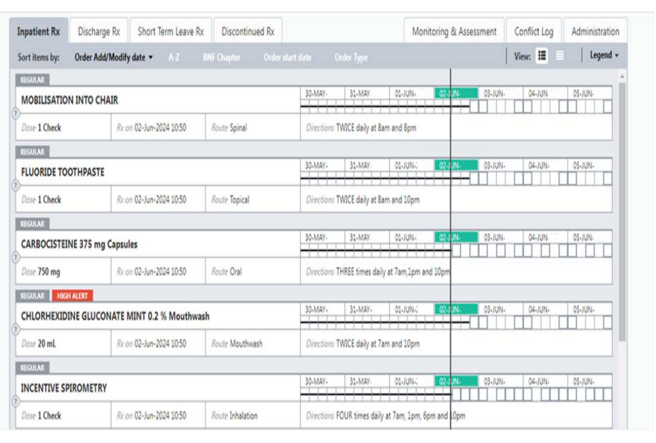

Figure 1: I-BREATHE components on the electronic medicine prescribing system.

All patients who underwent a major laparotomy at the NGOC from January 2019 to December 2019 (group A), and from October 2021 to October 2022 (group B) were captured in our analysis. Patients who had radical vulvectomies, laparoscopies and those patients who did not have the I-BREATHE bundle prescribed post-operatively were excluded. Demographic, pre-operative physical status, post-operative morbidity data, in-patient hospital stay and survival data were collected prospectively. The extent of surgery was assessed using the surgical complexity score, similar to the retrospective study. In addition, the European Perioperative Clinical Outcome (EPCO) definitions were taken to establish the incidence of different PPCs [8]. Chest infection was defined as prescription of antibiotics for a suspected respiratory infection and meeting one or more of the following criteria: New or changed sputum, new or changed lung opacities, fever, white blood cell count $>12 \times 10^9$ L^{-1}.

Outcome measures

The study compared the absolute incidence of postoperative chest infection; 30-day, 12-week and 1-year mortality; and in-hospital length of stay [both in Critical Care Unit (CCU) and ward].

In addition, in group B, absolute incidence of all PPCs was assessed along with the re-admission rate to either the High Dependency Unit (HDU) or Intensive Care Unit (ICU).

Statistical analyses were performed using Prism 9 for Macintosh Operating System (MacOS).

RESULTS

The entire study enrolled a total of 394 patients; 237 patients were included in the retrospective, pre-intervention cohort (group A) and 157 patients were included (Figure 2) in the prospective, post-intervention cohort (group B).

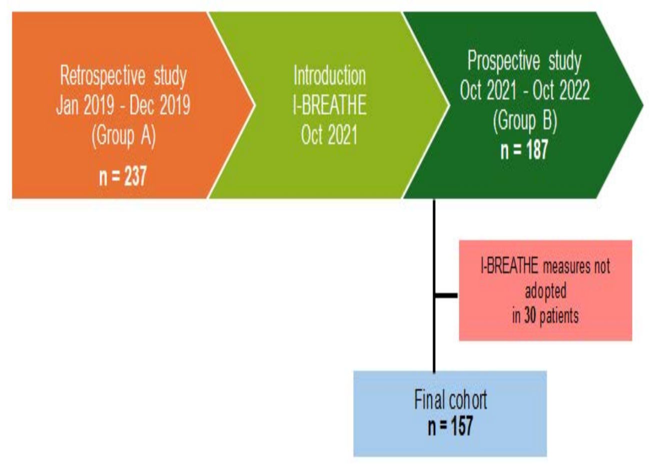

Figure 2: I-BREATHE time-line and flow chart of patient selection.

Demographic data

Both the groups were comparable in terms of age, sex, type of cancer and surgical complexity score (Table 1). The median age of patients in both the groups was 63 (p=0.57). Majority (56.6%) of patients in group A had an ASA physical status score of 2, whereas in group B, majority (57.8%) of patients had an ASA physical status score of 3, which was statistically significant. The most common cancer site was tubo-ovarian in both the groups. No statistically significant difference was noted between the groups with respect to the complexity of surgery (p=0.13); majority of patients having had surgeries with a low-level of complexity (52.1% in group A *vs.* 62.4% in group B).

Table 1: Demographic data.

Parameters		Control group (Group A) n=237	Case group (Group B) n=157	p value
Age (Median years)		63 (IQR 53-70)	63 (IQR 55-71)	0.57
American Society of Anaesthesiologist's (ASA) score	I	11/237 (4.7%)	4/157 (2.5%)	<0.01
	II	134/237 (56.6%)	62/157 (39.5%)	
	III	91/237 (38.2%)	91/157 (57.8%)	
	IV	1/237 (0.5%)	0/157 (0%)	
Smoking status	Non-smoker	159/237 (67.1%)	129/137 (82.2%)	<0.01
	Ex-smoker	53/237 (22.4%)	15/137 (9.5%)	
	Current smoker	23/237 (9.7%)	13/137 (8.3%)	
Complexity of surgery	Low	124/237 (52.1%)	98/157 (62.4%)	0.13
	Intermediate	92/237 (39.1%)	49/157 (31.2%)	
	High	21/237 (8.8%)	10/157 (6.4%)	

Note: IQR: Interquartile Range.

One other significant difference between both cohorts was the smoking status (p<0.01). The case group (group B) comprised of a larger proportion of non-smokers (82.2%), whilst the control group (group A) had a higher proportion of ex-smokers (22.4%) and smokers (9.7%).

Primary outcome 1: Chest infection

The incidence of chest infection was almost identical in both the groups (Table 2) with an incidence of 15.2% in group A and 15.3% in group B (RR: 1, 95% CI 0.63-1.62, p=0.98).

Table 2: Incidence of post-operative chest infection.

Control group (Group A)	Case group (Group B)	p value
36/237 (15.2%)	24/157 (15.3%)	0.98

A sub-group analysis has demonstrated a significant decrease in the incidence of chest infections in smokers and ex-smokers in group B, compared to group A (Table 3), with the incidence going down from 27.6% (group A) to 7.1% (group B) (RR: 0.26, 95% CI 0.065-1.032, p=0.03).

Table 3: Incidence of post-operative chest infections in smokers and ex-smokers.

	Control group (Group A)	Case group (Group B)	p value
Ex-smoker	53/237 (22.4%)	15/157 (9.5%)	<0.01
Current smoker	23/237 (9.7%)	13/157 (8.3%)	<0.01
Total	76/237 (32.1%)	28/157 (17.8%)	<0.01
Chest infections	21/76 (27.6%)	2/28 (7.1%)	0.03

There was a higher proportion of ex-smokers in group A (22.4%), compared to group B (9.5%) (p<0.01). Focussing on the control group, an association was found between smoking status and post-operative chest infection. Post-operative chest infection occurred more in women who smoked at the time of operation or had a history of smoking (27.7%) compared to non-smokers (9.3%) (p<0.01).

Primary outcome 2: Post-operative mortality

The 30-day postoperative mortality rates in both the groups were comparable (Table 4), with no statistical difference. This result was almost reproducible at 3-months and at 1-year (p=0.47).

Table 4: Table comparing 30 days, 90 days and 1 year mortality.

Time period	Control group (Group A)	Case group (Group B)	p value
Inpatient	2/237 (0.8%)	1/157 (0.6%)	0.91
<30 days	(1/237) (0.4%)	1/157 (0.6%)	0.77
<3 months	3/237 (1.3%)	1/157 (0.6%)	0.37
1 year	18/237 (7.6%)	17/157 (10.8%)	0.27

Primary outcome 3: In-patient hospital stay

There was a significant reduction in the total in-patient hospital stay and ward-based length of stay by a median of 2-days in group B compared to group A (Table 5 and Figure 3).

Table 5: Length of in-patient hospital stay.

Duration of stay	Control group (Group A)	Case group (Group B)	p value
Total stay (Median days)	8 (95% CI 7–9)	6 (95% CI 6–6)	<0.01
Critical Care Unit (CCU) (median days)	0.9 (95% CI 0.4–1)	1 (95% CI 0.8–1)	0.89
Ward (median days)	7 (95% CI 7–7.8)	5 (95% CI 4.9–5.1)	<0.01

Note: CI: Cumulative Index.

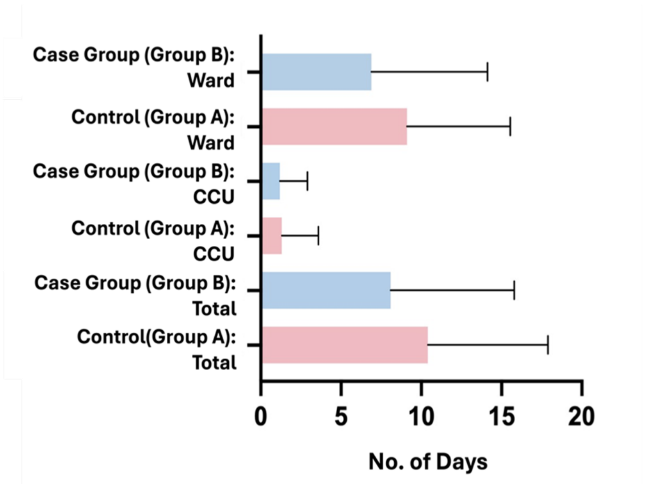

Figure 3: Figure comparing length of inpatient hospital stay.

Secondary outcome 1: Post-operative Pulmonary Complications (PPC)

Assessing the case group cohort (group B) for PPC, a total of 33 (21%) patients had radiologically proven reversible pre-operative pulmonary findings on chest imaging (Table 6). Out of total 157 patients, 51 patients had radiologically proven post-operative pulmonary complications; however, when comparing the pre- and post-operative imaging, 8 patients were found to have identical findings and therefore the true incidence of PPC was found to be 27.4% (43/157). The most common PPCs included chest infection, atelectasis and pleural effusions. There were 2 cases of respiratory failure and 1 case of pneumothorax.

Table 6: Incidence of Postoperative Pulmonary Complications (PPCs).

	n
Total number of patients in group B	157
Preoperative pulmonary findings on chest imaging	33 (21%)
Postoperative Pulmonary Complications (PPCs)	51 (32.5%)
Identical pre and post-operative pulmonary findings	8
Actual incidence of PPCs	43 (27.4%)

Group B patients were recruited during the Coronavirus (COVID-19) pandemic. All patients were tested for SARS-CoV-2 virus pre-operatively; only 3 patients tested positive for COVID-19 and their operation was postponed by 5 weeks. None of these patients developed PPCs. We found out that 2 patients developed COVID-19 in the immediate post-operative setting, of whom one developed mild atelectasis, seen on post-operative imaging but was deemed clinically insignificant.

Secondary outcome 2: Readmission to HDU/ICU

Readmission to HDU/ICU was seen in only 3 patients in group B, 2 of these patients required a second procedure due to a surgical complication and was admitted to HDU for monitoring, while 1 patient developed an aspiration pneumonia and required HDU admission for respiratory support.

DISCUSSION

The NGOC performs an average of 225 laparotomies annually. It is imperative that patients undergoing major surgery have robust perioperative care so as to reduce postoperative hospital stay and mortality among other quality indicators. Initiation of I-BREATHE, therefore, was viewed as a favourable step in this direction.

PPCs have considerable implications on resources, lengthen the inpatient hospital stay and have significant financial impact. Moreover, specifically to this cohort of patients this may also delay adjuvant treatment, resulting in significant implications to their overall response to treatment.

The I-BREATHE pathway was initiated following thorough literature research and discussions among the members of the SBU in our hospital, as there were significant financial implications involved. In the conceptual and planning phases, considering the capital injection required with this project and adverse financial climate, it was of utmost importance for the study to be deemed as tenable, by assessing its impact.

Our study showed that the introduction of I-BREATHE significantly reduced (i): Chest infections in smokers and ex-smokers ($p=0.02$) and (ii): The length of in-patient stay by a median of 2 days ($p<0.01$). However, the measures appear to have had no impact on the overall incidence of post-operative chest infection in the first year following its implementation.

The reasons for this persistent level of postoperative chest infections could be multifactorial. Starting with the demographic data, it appears, most patients in both the cohorts were of ASA physical status of 2 and 3. One also needs to consider that the radical surgeries performed in gynaecology-oncology are done on patients who are relatively deconditioned either due to the disease burden or secondary to the effects of chemotherapy. Many patients develop ascites and pleural effusion preoperatively, which considerably affect their respiratory functions. Some of the patients in our study were found to have pre-operative findings on chest imaging, most common of which was atelectasis. Moreover, due to the nature of the treatment options, disease progression and response to chemotherapy, an operation must be offered to this cohort of patients within a very short time frame. There is literature evidence, that radical surgery provided in this setting is associated with a high intra and post-operative morbidity [3]. Cytoreductive surgeries as part of the treatment of advanced ovarian cancer have higher than average incidence of PPC, reaching up to 32.3% in women having surgery performed on their diaphragms [5].

Most patients who underwent surgery in our centre had their anaesthetic preassessment only a few days prior to surgery. This is one of the most important reasons for failure to adequately optimise these patients, despite implementing the I-BREATHE pathway prior to their surgeries. There are other reasons as well such as, higher numbers of statistically significant unwell patients in terms of their ASA physical status in the post-intervention cohort.

Evidence in the literature highlights a divergence between outcome data from trials and routine clinical practice in preventing PPCs. There is no high-quality evidence supporting a particular intervention to reduce PPCs, however there is evidence supporting the use of intra-operative lung protective ventilation and goal directed haemodynamic strategies [13]. These strategies are already incorporated into the ERAS pathway for major surgeries in our hospital. The introduction of the I-BREATHE measures, however, complemented our baseline ERAS measures considerably, as we saw a significant reduction in chest infections in smokers and ex-smokers along with significant reduction in the length of in-patient postoperative stay. We believe, this is mostly due to the comprehensive preoperative measures in our pathway, which complements the rest of the ERAS measures, unlike other studies in literature.

One of our preoperative measures was the use of incentive spirometry. This is not shown to be of much benefit in preventing PPCs in literature. A recent meta-analysis highlights, that the main reason for this is believed to be the suboptimal use by patients because of lack of any supervision [14]. American Association for Respiratory Care's Clinical Practice Guidelines (CPG) on incentive spirometry recommends that it should be used with deep-breathing techniques, directed coughing, early mobilisation and optimal analgesia to prevent postoperative pulmonary complications [15]. However, the approach of its postoperative use under nurse supervision, to strictly improve patient compliance makes our study unique. Cassidy, et al. [7], used a similar protocol to ours to demonstrate reduction in postoperative pneumonia and unplanned intubations. We had further elements in our protocol in accordance with the 2021 perioperative guideline of the preoperative association, UK [10].

Use of a mucolytic agent to the routine perioperative care in a randomized placebo-controlled trial of 140 patients undergoing lobectomy for lung cancer [16] showed a significant reduction in the rate of PPC (6% *vs.*19%, p=0.02) and decreased length of hospital stay by 2.5 days (p=0.02). Another meta-analysis [17] showed a statistically significant benefit from a mucolytic in reducing the risk of PPCs, but the pooled sample size was small. We decided to add carbocisteine based on these evidence, but it is difficult to conclude whether this measure on its own was the reason for the significant favourable outcomes of our study.

I-BREATHE centres on encouraging a culture of education and improvement. The aim was to introduce an easy-to-remember, standardized approach for our patients to receive optimal care during arguably one of the most important events in their lives. In this way, not only did we develop practices advocating for healthy lifestyle choices but we reinforced an institutional culture change promoting excellence and advocacy.

Limitations

The limitations in our study included a smaller sample size in the post-intervention cohort when compared to the pre-intervention cohort. We did not account for the effects of neo-adjuvant chemotherapy. We were also unable to assess compliance with preoperative incentive spirometry. Due to the coronavirus pandemic, most patients resorted to staying indoors which could have resulted in them being more deconditioned despite our efforts with I-BREATHE, although this is difficult to quantify.

CONCLUSION

The addition of a structured peri-operative respiratory optimisation bundle within the ERAS protocol in high-risk patients having surgery for gynaecological malignancy has been seen to be very effective in the cohort of patients who smoke or used to smoke with a significant reduction in the incidence of chest infections. Moreover, the implementation of these strategies has shown a significant reduction on in-patient length of stay. In view of the limitations of the study more research is needed to definitively recommend our initiative to all types of high-risk surgeries.

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