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Enhanced recovery after surgery in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: national survey of peri-operative practice by Indian society of peritoneal surface malignancies

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Abstract

Objectives: The Enhanced recovery after surgery (ERAS) program is designed to achieve faster recovery by maintaining pre-operative organ function and reducing stress response following surgery. A two part ERAS guidelines specific for Cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) was recently published with intent of extending the benefit to patients

with peritoneal surface malignancies. This survey was performed to examine clinicians' knowledge, practice and obstacles about ERAS implementation in patients undergoing CRS and HIPEC.

Methods: Requests to participate in survey of ERAS practices were sent to 238 members of Indian Society of Peritoneal Surface malignancies (ISPSM) via email. They were requested to answer a 37-item questionnaire on elements of preoperative (n=7), intraoperative (n=10) and postoperative (n=11) practices. It also queried demographic information and individual attitudes to ERAS.

Results: Data from 164 respondents were analysed. 27.4 % were aware of the formal ERAS protocol for CRS and HIPEC. 88.4 % of respondents reported implementing ERAS practices for CRS and HIPEC either, completely (20.7 %) or partially (67.7 %). The adherence to the protocol among the respondents were as follows: pre operative (55.5–97.6 %), intra operative (32.6–84.8 %) and post operative (25.6–89 %). While most respondents considered implementation of ERAS for CRS and HIPEC in the present format, 34.1 % felt certain aspects of perioperative practice have potential for improvement. The main barriers to implementation were difficulty in adhering to all elements (65.2 %), insufficient evidence to apply in clinical practice (32.4 %), safety concerns (50.6 %) and administrative issues (47.6 %).

Conclusions: Majority agreed the implementation of ERAS guidelines is beneficial but are followed by HIPEC centres partially. Efforts are required to overcome barriers like improving certain aspects of perioperative practice to increase the adherence, confirming the benefit and safety of protocol with level I evidence and solving administrative issues by setting up dedicated multi-disciplinary ERAS teams.

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Introduction

The multimodality treatment of cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC) combines radical surgery with circulation of heated chemotherapy in the peritoneal cavity for selected patients with Peritoneal surface malignancies (PSM) [1].

This radical surgery induces metabolic and inflammatory responses, associated with higher morbidity, prolonged in-patient stay and longer recovery compared to other gastrointestinal and gynaecological oncological procedures. Enhanced recovery after surgery (ERAS) protocols represent fundamental shifts in surgical practice designed to achieve early recovery by maintaining preoperative organ function and reducing the profound stress response following surgery [2–4]. A survey showed CRS and HIPEC has been well accepted by the oncological community [5].

ERAS programs offer a practical, evidence based, patient-centric practices to eliminate ambiguities, disparities to achieve best surgical care. There is already significant evidence indicating that ERAS protocols leads to improved outcomes in major abdominal and extra-abdominal surgical procedures, while being safe [5–13].

There is a wide acceptance to ERAS in western countries, whereas in the developing countries, ERAS programs are still facing considerable challenges for application [14]. Incorporation of pre-, intra-, and postoperative practices of the ERAS pathway in the management of patients undergoing CRS-HIPEC causes synergistic effect of early reversal of the pathophysiological responses and thereby hasten recovery and reduce complications. Preliminary experience of partial application of ERAS in CRS and HIPEC patients showed a reduction in overall intravenous fluids, postoperative narcotic use, complication rates [15–17].

Recently Hubner et al. published the formal ERAS guidelines specific to CRS and HIPEC with several key elements of including preoperative counselling, optimization of nutrition, standardized analgesic and aesthetic regimens, early mobilization and special consideration for HIPEC [18, 19]. This formal ERAS protocol represents a significant change in practice for CRS and HIPEC, but also poses a challenge for adherence and compliance. It is

unclear to what degree ERAS guidelines are implemented in HIPEC centres of excellence.

The aim of this study was to evaluate utilization of ERAS in CRS and HIPEC, assess knowledge, current practices and barriers to adherence.

Methods

The survey was submitted to all the members of Indian society of peritoneal surface malignancies (ISPSM) via email, as extracted from the membership directory of the association. Reminders were sent to the non-responders via e-mail. The questionnaire was developed after extensive research for various elements of the ERAS protocol. The questionnaire was pilot-tested among the ERAS specialists and oncologists within our institution for assessment and changes were made based on feedback.

The questionnaire had 37 items and was divided into five sections. Section one dealt with the demographics and their awareness of ERAS protocols. The second, third and fourth sections consisted of questions investigating elements of preoperative (n=7), intraoperative (n=10) and postoperative (n=11) practices and their extent of implementation. Non-essential components of the protocol were not included in the questionnaire. The last part assessed the individual attitudes and barriers for implementation and adherence Figure 1.

A descriptive statistical analysis was carried out and described quantitative and qualitative data according to means ($\pm$ standard deviation), medians (range) and percentages. The percentages were calculated over all the responses received for each question. Percentages and frequencies were used for the descriptive analysis of the data.

Results

Out of 238 active surgical members of ISPSM who were contacted for the survey, 164 (68.9 %) replied with completed questionnaire. We compiled and analysed the results from the participants (Figure 2).

Demographic characteristics of survey respondents are shown in Table 1. Our nation has a huge variation in the types of institutes delivering healthcare in our country, 23.1 % of the doctors practice in a public medical research university hospitals while rest are involved in private care. Although not officially registered with ERAS society 95.7 % were already implementing ERAS for other surgical specialities. Eighty-eight percent of respondents reported implementing ERAS practices for CRS and HIPEC, completely (20.7 %) or partially (67.7 %).

Questionnaire responses for pre-operative and intra operative components of ERAS for CRS and HIPEC guidelines are shown in Tables 2 and 3. Routine bowel preparation with oral antibiotics was reported by 62.2 % of respondents. Pre-operative fasting for solids up to 8 h

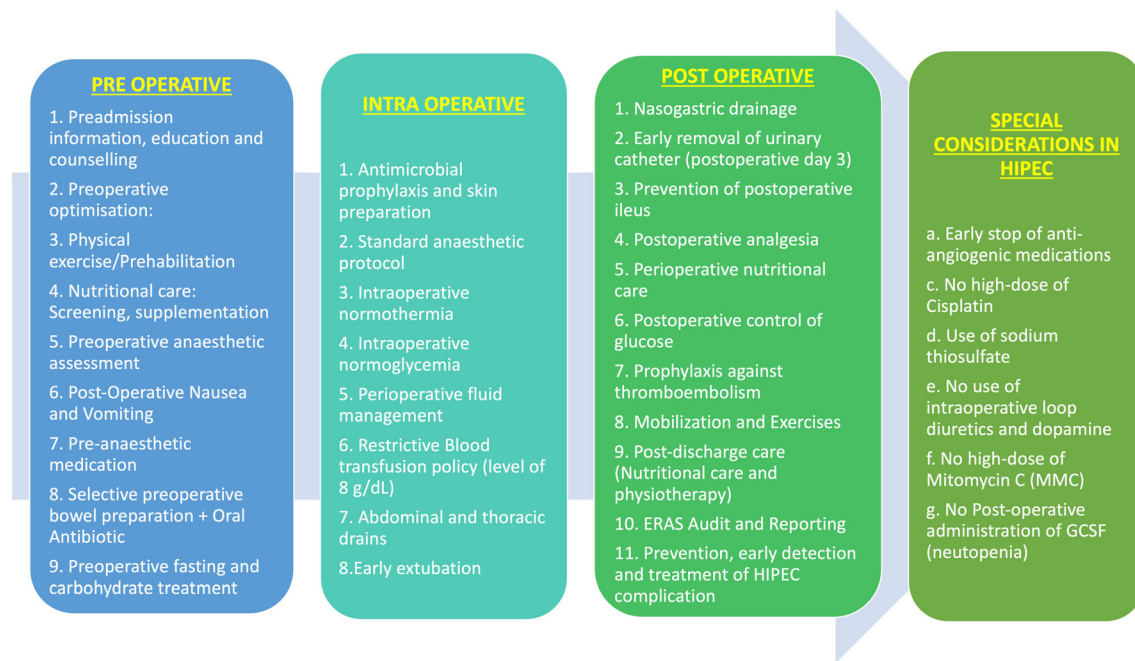


Figure 1: Components of ERAS for CRS and HIPEC.

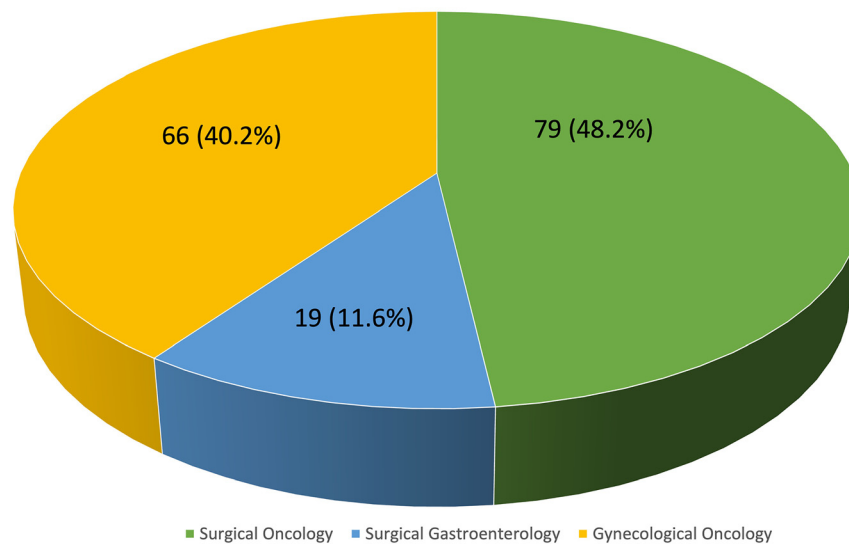


Figure 2: Subspecialty of the survey respondents.

before surgery was reported by nearly 55.5 % of respondents; 18.3 % of respondents said they allowed clear liquids up to 2 h before surgery, 58 % 2–6 h before surgery, and only 26.2 % reported carbohydrate loading too. Pre-operative and intra-operative deep vein thrombosis prophylaxis was administered by more than 80 % of respondents. Low molecular weight heparin was the most common modality used for this purpose (71.3 %), while rest of respondents reported using stockings or pneumatic compression devices. In the anaesthetic considerations of

the protocol total intravenous anaesthesia (59.1 %) with protective mechanical ventilation (71 %) was most commonly followed while invasive cardiac monitoring (32.6 %) was not routine. Goal-directed fluid therapy was reported by only 60.4 %. Regional anaesthesia was employed by most respondents (84.8 %) with epidural analgesia (59.1 %) being most popular followed by Transversus abdominis plane (TAP) block in 16.5 % followed by NSAIDs or Paracetamol (15.2 %). More than 50 % preferred to place drains routinely in all cases.

Table 1: Demographic characteristics of survey respondents.

Sl	Parameters	n=164	%
1	What is the type of hospital where you practice?		
	– Medical college	38	23.1
	– Private teaching institution	67	40.9
	– Private hospital	59	35.0
2	What is your specialty?		
	– Surgical oncology	79	48.2
	– Surgical gastroenterology	19	11.6
	– Gynaecologic oncology	66	40.2
3	What's your experience in performing CRS + HIPEC?		
	– <2 years	26	15.9
	– 2–5 years	70	42.7
	– >5 years	68	41.4
4	Are you aware of dedicated guidelines of enhanced recovery after surgery (ERAS) for CRS + HIPEC?		
	– Yes	45	27.4
	– No	129	72.6
5	Do you follow ERAS for CRS + HIPEC?		
	– Yes	34	20.7
	– Partially	111	67.7
	– No	19	11.6
6	Peri-operative care protocols implemented in your institution for CRS HIPEC are based on guidelines set by?		
	– MDT experts based on extrapolation	130	79.3
	– ERAS recommendations	34	20.7
7	What is the benefit of implementation of ERAS protocol in CRS HIPEC according to you ? (multiple choices possible)		
	– Multimodal rehabilitation and reduce complications	137	83.4
	– Clinical research	61	37.2
	– Reduce costs	29	17.7
	– Reduce hospital stay	112	68.3
	– Not sure	29	17.7
8	Are you registered with ERAS society with dedicated ERAS co-ordinator? (Do you follow ERAS audit and reporting?)		
	– Yes	12	7.3
	– No	152	92.7
9	Does your department offer ERAS for other surgical specialties?		
	– Yes	41	25
	– Partially	116	70.7
	– No	7	4.3

Table 4 shows the responses for the post-operative components of the guidelines. Nasogastric tube usage was common, reported to be used 'always' and 'sometimes' by 45.7 and 35.4 % respectively. Majority of respondents attempted for early indwelling catheter removal (78 %). Among strategies to hasten the return of bowel activity, chewing gum (64 %) and laxatives (29.9 %) were used commonly. Nearly 36 % of respondents indicated that they did not routinely employ substances to prevent post-operative ileus. Early post-operative diet initiation was not adhered by nearly three-fourth of the respondents, with clinical exam being the main indicator for resumption of

Table 2: Questionnaire responses for pre-operative components of ERAS guidelines for CRS and HIPEC.

Sl	Parameters	n=164	%
1	Preadmission information, education and counselling		
	– Yes	160	97.6
	– No	4	2.4
2	Preoperative optimisation: Alcohol and smoking cessation		
	– 4 weeks	21	12.8
	– <4 weeks	143	87.2
3	Do you perform prehabilitation and nutritional care		
	– Yes	103	62.8
	– No	61	37.2
4	Do you give pre-operative antiemetic drugs for post-operative nausea and vomiting (PONV):		
	– Yes	94	57.3
	– No	19	11.6
	– Not sure	51	31.1
5	Preoperative bowel preparation + oral antibiotic		
	a. Always	102	62.2
	b. Selective	62	37.8
6	What is the preoperative fasting protocol in your institute?		
	– 2 h for clear fluids, 6 h for solids	30	18.3
	– 2 h for clear fluids, 6 h for solids with carbohydrate loading – Nil per oral since midnight	43	26.2
		91	55.5
7	Pre-operative DVT prophylaxis		
	a. Unfractionated heparin	0	0
	b. Low molecular weight heparin	117	71.3
	c. Stockings	11	6.7
	d. Pneumatic compression device	4	2.5
	e. No	32	19.5

diet. Fluid overload avoidance and monitoring was not done regularly by the clinicians (73.2 %). Patients were ambulated on the day of surgery by 10.4 % of respondents, while 63.4 % reported that patients typically ambulated on the first post-operative day.

Attitudes to ERAS in CRS and HIPEC

65.9 % of clinicians responded that they would implement the published ERAS protocol in patients undergoing CRS and HIPEC without modifications. Overall, 65.2 % felt that ERAS protocols is a useful tool but few elements are difficult to adhere to. The other issues of concern for full implementation were safety (50.6 %), lack of evidence (35.4 %) and administrative issues (47.6 %). 84 % felt that ERAS protocols decreased hospital stays and 62.8 % re-admission rates. ERAS practices improved overall patients' satisfaction according to 40.2 % of respondents, and 54.3 % felt that ERAS pathways improved patient outcomes. The surgeons were asked to

Table 3: Questionnaire responses for intra-operative components of ERAS guidelines for CRS and HIPEC.

SI	Parameters	n=164	%
1	What type of general anaesthesia is usually included in the protocol in your hospital?		
	a. Total intravenous anaesthesia with propofol	67	59.1
	b. Inhalational agents based	38	23.2
	c. Not definite	29	17.7
2	Do you use routine protective mechanical ventilation?		
	a. Yes	118	71
	b. No	0	0
	c. Not sure	46	28
3	Do you use cardiac output monitoring routinely?		
	a. Yes	37	32.6
	b. No	127	67.4
4	Do you use any modalities to measure and maintain intraoperative normothermia?		
	a. Yes	164	100
	b. No	0	0
5	Do you perform goal-directed fluid management during surgery?		
	a. Yes, goal-directed therapy protocol	99	60.4
	b. Not sure, at discretion of anaesthesia team	58	35.4
	c. No	7	4.2
6	Do you perform restrictive blood transfusion policy (threshold level of 8 g/dL)		
	a. Yes	71	43.3
	b. No	93	56.7
7	Do you use regional analgesia?		
	a. Epidural	97	59.1
	b. Spinal adjunct	15	9.1
	c. Nerve blocks (erector spinae/transversus abdominis block)	27	16.5
	d. No	25	15.3
8	Do you place abdominal and thoracic drains?		
	a. Always	85	51.8
	b. Sometimes (bowel resection, splenectomy, bladder repair)	65	39.6
	c. No	14	8.6
9	Do you attempt for early extubation regularly?		
	a. Yes	70	62.7
	b. No	55	13.5
	c. Not sure	39	23.8
10	Do you avoid use of postoperative antibiotic prophylaxis?		
	a. Yes	28	17.1
	b. No	89	54.3
	c. Not sure	47	28.4

evaluate the components of ERAS that are most effective interventions in improving the outcomes and responses were Intraoperative goal directed therapy (82.9 %), perioperative feeding practices (78 %) and early aggressive mobilisation (73.1 %). According to the respondents the elements that are difficult to implement included avoidance of mechanical bowel preparation (58 %), avoidance of drains

(81.7 %), avoidance of post op fluid overload (48.1 %), regular diet initiation (73.2 %) Table 5.

Discussion

With the availability of the formal ERAS CRS-HIPEC guidelines, we wanted to characterise the prevailing pattern of perioperative practice among specialist surgeons performing CRS and HIPEC. This is the first survey among HIPEC super specialists that has examined the degree of ERAS implementation and assess the knowledge attitudes and practice patterns based on published formal protocol. Previous surveys were based on a working ERAS guidelines which was extrapolated information from colorectal and gynaecological ERAS practices. Our survey revealed that ERAS for CRS and HIPEC was more widely adopted by surgeons with institutions already having dedicated ERAS program.

Despite majority already implementing ERAS protocol completely or partially among other surgical branches, we found that there were variations in the pattern of application during clinical practice. Among the ERAS protocols for CRS and HIPEC, pre and intra operative elements were the best-adhered components. Pre-admission rehabilitation, preoperative nutritional screening and care, multimodal prophylaxis for postoperative nausea and vomiting (PONV), DVT prophylaxis, maintenance of intraoperative normothermia, anaesthesia induction and ventilation, regional anaesthesia avoid use of opioids, early removal of urinary catheter, were well adopted. However, there were many practices followed by the respondents which would be considered to be in contradiction with the ERAS guidelines. Elective mechanical bowel preparation, pre-operative fasting protocol, cardiac output monitoring, goal-directed intravenous fluid administration were relatively less well-adopted.

Evidence and ERAS guidelines have supported the avoidance of routine mechanical bowel preparation and use only for left sided colonic resections, particularly due to adverse outcomes such as hypovolemia and dehydration and the fact that it does not decrease post-operative morbidity [6]. But nearly 62 % of the surgeons in the survey still insist on it routinely, probably because in CRS most patients need multi visceral resections and there is no way to predict to whom we perform only left sided resections [20].

Preoperative fasting of 2 h for clear fluids and 6 h for solid meals was followed by most surgeons, in accordance with the ERAS protocol. But few respondents still preferred overnight fasting, probably as per the guidelines issued by the Indian Society of Anaesthesiologists based on distinct

Table 4: Questionnaire responses for post-operative components of ERAS guidelines for CRS and HIPEC.

SI	Parameters	n=164	%
1	Do you avoid use of post-operative nasogastric drainage?		
	a. Yes	31	18.9
	b. Sometimes (bowel resection, lesser omentectomy)	58	35.4
	c. No	75	45.7
2	Do you follow early removal of urinary catheter (<post op day 3)		
	a. Yes	87	53
	b. Sometimes	41	25
	c. No	36	22
3	Which postoperative strategies do you use to accelerate the recovery of gastrointestinal function? (Choose all that apply)		
	a. Chewing gum/Coffee	105	64
	b. Mu-opioid receptor antagonists	18	11
	c. Laxatives	49	29.9
	d. Prokinetics: Erythromycin	11	6.7
	e. Not routinely	59	36
4	Which method of regional analgesia do you prefer for postoperative pain control?		
	a. Epidural analgesia	88	53.6
	b. Abdominal blocks	25	15.3
	c. Combination analgesia (paracetamol, NSAIDs)	42	25.6
	d. Opioids	9	5.5
5	When do you initiate post-operative regular diet?		
	a. On POD 1	19	11.6
	b. >POD 2	23	14
	c. Based on clinical exam (bowel sounds/Passing of flatus)	122	74.4
6	Do you use pre-emptive parenteral nutrition?		
	a. Yes	146	89
	b. No	18	11
7	Do you actively monitor and avoid post-operative fluid overload?		
	a. Yes	44	26.8
	b. No	68	41.5
	c. Not sure	52	31.7
8	Prophylaxis against thromboembolism		
	a. Till mobilization	25	15.2
	b. Till hospitalization	111	67.7
	c. 1 month	28	17.1
9	When do you start post-operative ambulation (average start time)		
	a. Day of surgery	17	10.4
	b. POD1	43	63.4
	c. >POD2	104	26.2
10	What is the duration of post operative physical exercises (>POD 2)		
	a. 6 h	7	4.3
	b. <6 h	36	22
	c. Physiotherapist discretion	121	73.7
11	Do you follow strategies for prevention, early detection and treatment of HIPEC complication		
	a. Early stop of anti-angiogenic medications	160	97.5
	b. No high-dose of cisplatin	129	78.6

Table 4: (continued)

SI	Parameters	n=164	%
	c. Use of sodium thiosulfate	31	18.9
	d. No use of intraoperative loop diuretics and dopamine	48	29.3
	e. No post-operative administration of GCSF (neutopenia)	129	78.6

Table 5: Respondents' attitudes towards ERAS practices.

SI	Parameters	n=164	%
1	Would you implement the published ERAS protocol in all your patients undergoing CRS + HIPEC without modifications?		
	a. Yes	108	65.9
	b. No	56	34.1
2	Barriers of implementing ERAS in CRS + HIPEC (choose all that apply)		
	a. Beneficial but difficult to adhere to all elements	107	65.2
	b. Evidence to support is insufficient	58	35.4
	c. Safety concerns	83	50.6
	d. Administrative issues	78	47.6
3	What are the benefits of implementing ERAS for CRS + HIPEC (choose all that apply)		
	a. Improves patient outcome: Hospital stay and ICU stay	138	84.1
	b. Reduces re-admission rates	103	62.8
	c. Reduces complication	89	54.3
	d. Improves patient satisfaction	66	40.2
4	What are the interventions which make the current ERAS protocol for CRS HIPEC effective? (Choose all that apply)		
	a. Early removal of indwelling catheter	91	55.5
	b. Intra operative goal directed therapy	136	82.9
	c. Short NPO duration, carbohydrate loading, early oral feeding and nutritional management	128	78
	d. Early aggressive mobilisation	120	73.1
	e. Ileus prevention strategies	39	23.8
	f. Epidural and postoperative pain management	85	51.8
5	What are the elements of ERAS guidelines that are difficult to implement? (Choose all that apply)		
	a. Mechanical bowel preparation avoidance	95	58
	b. Oral regular diet initiation on POD1	120	73.2
	c. Avoidance of post-operative antibiotics	108	65.8
	d. Avoidance of post-operative fluid overload	79	48.1
	e. Avoidance of naso gastric tubes	88	53.6
	f. Avoidance of intraperitoneal drains	134	81.7

eating habits of Indian population [21]. Oral consumption of complex carbohydrate, 2 h before induction of anaesthesia reduces the postoperative insulin resistance and improves postoperative outcomes [22]. Despite a strong recommendation in favour by ERAS protocol, only 26.2 % of the respondents

reported to be following it. The poor implementation can be related to fear of aspiration. This highlights the need for customising the version of the ERAS protocol for the Indian population or educating the anaesthetists.

Surgeons agreed that the improvement in outcomes is not an effect of one particular element of the protocol, but rather an aggregation of marginal gains from all the elements. Even though it is not always possible to fully adhere to the protocol, as a whole they are proven to work, which is clearly confirmed in our analysis. The intervention which was most effective was intra operative goal directed therapy. Balanced fluid therapy as a single element lowers the morbidity rate, shortens LOS or decreases time to first flatus [23, 24].

Although there is a trend towards use of multimodal optimisation, the majority of the surgeons were still adhering to conventional post-operative care with variations in elements of ERAS guidelines. Abdominal and thoracic drains, Avoid use of antibiotic prophylaxis, early nasogastric tube removal, post-operative fluid overload monitoring and avoidance, initiation of early postoperative feeding and aggressive active mobilisation. However this practice has not been adopted in most of the surgeons. This could be attributed to many factors like pulmonary and cardiac comorbidities, extent of the surgery such as resection of the viscera (gastric/intestinal resection, Omentectomy, Diaphragmatic resection, splenectomy), amount of blood loss and duration of surgery.

The avoidance of post-operative fluid overload was not in practice among majority of respondents. The study demonstrates that certain traditional aspects of surgical care, such as the use of drains and nasogastric tubes and reliance on bowel sounds persists. Although routine NG decompression is not recommended [3]. In extensive upper abdominal procedure for CRS is like total supra colonic omentectomy, Lesser omentectomy, gastric resections or splenectomy is performed can lead to delayed gastric emptying necessitating post op NG drainage [25].

Guidelines have recommended against the routine use of peritoneal drains. Placement of drains can stimulate serous fluid production, and may lead to an increased risk of surgical-site infection and adhesions without any benefit of early detection of anastomotic leak [26, 27]. After CRS and HIPEC the possibility of intraperitoneal collections and abscess is higher and therefore most surgeons prefer placement of intraperitoneal drains.

65 % respondents in our survey stated the biggest barrier for implementation of ERAS was ensuring adherence and managing compliance. This is possibly because institutions without dedicated ERAS program have challenges in creating an effective 'ERAS team' (surgeon, anaesthetist, and nursing

care givers), which is required for optimal implementation, adherence and compliance [28].

The main hindrances faced in the implementation of ERAS as per our survey respondents were safety issues, lack of level I evidence and administrative issues. While the majority of respondents' attitudes were in favour of ERAS, more than half of respondents indicated that they felt that ERAS was associated with adverse outcomes and did not feel comfortable with few elements of the protocol. The main concerns was regarding NPO status, avoidance of NG tubes and drains and early initiation of regular diet. Although many studies have demonstrated safety, this has been with colorectal or gynaecological surgery where minimally invasive surgeries are very common. In CRS and HIPEC this is very different as the sheer extensive grade of surgery (peritonectomy and multivisceral resections) will lead to many physiological changes which makes few elements of guidelines not practical. This might be also be attributed to the fact of lack of studies of ERAS for CRS and HIPEC. There is also institutional variation in several perioperative practices, whereby hospitals already offering ERAS for other surgical specialities with well trained staff and co-ordinated effort from allied departments. One of the most important aspects is multidisciplinary and clinical support. The ERAS team includes pre-admission staff, dieticians, nurses, physiotherapists, social workers, occupational therapists and doctors. All team members must be familiar ERAS principles and be motivated and educated to carry out the program; they must be able to overcome traditional concepts, teaching and attitudes towards perioperative care. Increasing awareness among allied clinical departments, staff members of the hospital and demonstrating the cost benefits, patient satisfaction the may help in overcoming the administrative issues [29, 30].

There were some limitations to our study. First, the survey-based study represents clinicians' opinions and may not represent real world practice. The respondents included only surgeons and did not include anaesthetists, intensive care specialists or nursing care providers. Due to the extensive nature of the ERAS protocol, all the components of ERAS could not be followed by the respondents.

Conclusions

Our survey has shown that ERAS has have been adopted among most surgeon members of ISPSM, although certain aspects of perioperative practice have potential for improvement. The practice of ERAS should be encouraged in all. Conventional practices, traditional attitudes and non-intuitive protocols need to change and clinical staff have to

adapt. Survey demonstrated that certain aspects of enhanced recovery are more commonly in practice by centres already following ERAS principles for other specialities. The dilemma is not only the implementation of ERAS protocols but also to improve the protocol and to achieve high compliance.

ERAS is a multidisciplinary concept, and a coordinated effort is needed between various specialities to improve penetration of the ERAS protocol in CRS and HIPEC. Training and formation of dedicated team is imperative. More robust clinical evidence is needed to convince the clinicians to include all elements of protocol to systematically incorporated into ERAS practices. Few aspects may be difficult to implement in all patients and more evidence is needed to recommend their routine use.

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