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EDITORIAL

Enhanced recovery for colorectal surgery: Practical hints, results and future challenges

Gianpiero Gravante, Muhammad Elmussareh

Gianpiero Gravante, Department of Colorectal Surgery, Pilgrim Hospital, Boston, Lincolnshire PE21 9QS, United Kingdom
Muhammad Elmussareh, Department of Surgery, Leicester Royal Infirmary, Leicester, Leicestershire LE1 5WW, United Kingdom
Author contributions: Gravante G and Elmussareh M directly participated in the study in terms of contributions to conception and design, acquisition of data, and analysis or interpretation of data and both wrote the manuscript and revised it critically.
Correspondence to: Gianpiero Gravante, MD, Department of Colorectal Surgery, Pilgrim Hospital, Castle Road, Boston, Lincolnshire PE21 9QQ, United Kingdom. ggravante@hotmail.com
Telephone: +44-11-62588244 Fax: +39-6-233216592
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Abstract

Enhanced recovery after surgery (ERAS) protocols are now achieving worldwide diffusion in both university and district hospitals with special interest in colorectal surgery. The optimization of the patient's preoperative clinical conditions, the careful intraoperative administration of fluids and drugs and the postoperative encouragement to resume the normal physiological functions as early as possible has produced results in a large amounts of studies. These approaches successfully challenged long-standing and well-established perioperative managements and finally achieved the status of gold standard treatments for the perioperative management of uncomplicated colorectal surgery. Even more important, it seems that the clinical improvement of the patient's clinical management through ERAS protocols is now reaching his best outcomes (length of stay of 4-6 d after the operation) and therefore any further measures add little to the results already established (i.e., the adjunct of laparoscopic surgery to ERAS). Still dedicated meetings and courses around the world are exploring new aspects including the improvement the preoperative nutrition status to provide the energy necessary to face the surgical stress, the preoperative individuation of special requirements that could be properly addressed before the date of surgery and therefore would reduce the number of unnecessary days spent in hospital once fully recovered (i.e., rehabilitation, social discharges), and finally the development of an important web of out-of-hours direct access in order to individuate alarm symptoms in those patients at risk of complications that could prompt an early readmission.

Key words: Enhanced recovery; Fast track; Colorectal surgery; Length of stay

Peer reviewer: Dr. Imtiaz Wani, Department of Surgery, SMHS Hospital, Srinagar, Kashmir 190009, India

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INTRODUCTION

Enhanced recovery after surgery (ERAS) is a series of perioperative protocols that aim to improve the patient's ability to face major operations and consequently ameliorate his postoperative recovery[1]. ERAS interventions focus on those key factors that usually keep patients in hospital and make them dependent on drugs and specialist assistance following uncomplicated surgery, namely the need for parenteral analgesia, the administration of intravenous fluids and confinement to bed[2]. Pillars of ERAS protocols cover all the perioperative phases by removing or decreasing the influence of such factors and promoting good habits that favour the recover of

physiological functions. Therefore, they avoid mechanical bowel preparations (MBPs) and preoperative fasting before surgery and administer high carbohydrate meals until few hours from the operation; they limit the administration of fluids tailoring them to the real patient' s necessities during surgery; they encourage the resumption of an oral diet and early mobilization after surgery as well as they decrease the use of regular opioids using pain killers with less impact on the gut function[2-5].

Since their introduction ERAS protocols faced large resistances because they targeted diffuse and time-validated clinical practices[6]. These were mostly based on tradition, personal experiences, and surgical teaching that helped their historical perpetration. However, the growing amount of data available has showed now how such practices were not necessary or contributed to the adverse effects of the surgical trauma. As a result the most immediate and visible effect of ERAS introduction is a significant shortening of the length of stay (LOS) in hospital and therefore a better redistribution of the available resources. Nowadays ERAS is routine in large university hospitals and is also spreading to district general hospitals with special interests in colorectal operations[7].

PROTOCOLS

Preoperative period

Different ERAS protocols are available for colorectal surgery (Table 1). In most of them patients receive a preoperative functional assessment in order to target the eventual specific postoperative requirements and provide him with an adequate care organised for his necessities. Also, the preoperative visit would counsel the patients about the purposes and goals of the enhanced recovery addressing their expectations from the surgical recovery and reassuring them about the purposes of the early discharge. This should not be perceived as an economic necessity, but, when feasible and appropriate, is an integrated part of the treatment that avoids prolonged stays in wards where the risk of transmitted infections is significant.

Various protocols evaluate the nutritional status of patients, and, when necessary, oral supplementation is administered. Patients are usually fed until two hours before induction to avoid unnecessary consumption of body nutrients[8-11]. Few studies specified the necessity of a carbohydrate loading to prepare the body to the surgical stress and this seems a promising field of research[8,9]. Most studies do not administer MBP but some of them still use it in case of high-risk anastomosis (i.e., left-sided colonic resections)[12-17]. Only few authors use MBP routinely nowadays[10,18,19].

Intraoperative period

The leading concept of ERAS for the intraoperative phase is to administer drugs and fluids to the minimum dose effectively required by the patient and the operation. The avoidance of excessive amounts of drugs during surgery prevents their postoperative side-effects and accelerates the recovery. In this view, some authors administer short-acting anaesthetics to tailor them to the ongoing surgical necessity and to stop them quickly when not required anymore[8,9,11]. Similarly, intraoperative fluids are carefully given ranging from 1000 mL crystalloids and 500 mL colloids[8,9] to a total of 2000 mL crystalloids[12-16]. Intraoperative hypothermia is always avoided (Table 1).

Another important concept is that the control of postoperative pain already starts with some simple but effective intraoperative measures. Thoracic epidural can easily control postoperative pain after the operation. The simple infiltration of local anesthetics in the largest wound at the end of surgery also contribute to a better pain control[12-16]. Finally, transverse or curved incisions should be preferred when feasible[20-23].

Postoperative period

In the postoperative period the general purpose of ERAS is to resume the normal physiological activities and to stop the artificial introduction of fluids and drugs as soon as tolerated by patients. In this view, the administration of intravenous fluids, already restricted during the operation, is definitely discontinued during the first postoperative hours in most studies[18]. Early oral feeding is started in the form of free fluids up to 800 mL[8,9,20-23], a soft diet[24,25], or oral nutritional supplementation (one high-protein/high-calorie drink)[12-16] along with regular antiemetics to prevent nausea[8,9,17,18]. To facilitate the resumption of bowel motility patients avoid regular opioids (still used for breakthrough pain), receive oral analgesia in the form of regular Paracetamol and non-steroidal antinflammatory drugs (with proton-pump inhibitors coverage)[26] and are encouraged to sit out in chair. Rarely patients are encouraged to start walking after the operation[19] although this target is usually achieved on the first postoperative day[24,25]. Nasogastric tubes or drains are avoided to facilitate mobilisation and feeding but few authors maintain them after pelvic surgery[19].

During the 1st postoperative day the diet is built up to a normal meal or three high-protein/high-calorie drinks[12-16], and some laxatives may be used to stimulate the bowel function[12-16]. The urinary catheter is removed in most colonic resections exception made for pelvic surgery where it can last until the 2nd or 3rd postoperative day[12-16,19]. On the second postoperative day the epidural is removed and by the 4th or 5th day patients are evaluated for discharge.

RESULTS

LOS and readmission rates

Nine studies compared LOS between ERAS and conventional care (CC) in colorectal surgery[7,9,14,17,18,20,22,27,28] (Table 2). In all of them the LOS was reduced of about 54%-61% following ERAS protocols[14] and the ERAS

Table 1 Types of enhanced recovery after surgery protocols adopted

Ref.	Preoperative	Intraoperative	Postop (first 24 h)	Day 1	Day 2	Day 3	Day 4	Additional comments
Kahokehr *et al*[8,9]	Nutritional supplementation NBM two hours preinduction Carbohydrate loading No bowel preparation Functional assessment and goal setting	Thoracic epidural Short acting anaesthetics Intraoperative fluids: 1000 mL of crystalloid and 500 mL of colloid Prophylactic antiemetics at induction (Dexamethasone) No drains or NG tubes	All IV fluid stopped Prophylactic antiemetics Early oral feeding Nutritional supplementation No opioids	Removal of urinary catheter	Removal of epidural			Early mobilization and physiotherapy
King *et al*[12-14]	Nutrition supplementation	Thoracic epidural	Free fluid	All IV fluid stopped	Removal of epidural Regular NSAIDS	Removal of urinary catheter for rectal resections		Aim for discharge on day 3 for colonic or day 5 for rectal resection
Blazeby *et al*[15]	Optimised pre-morbid health status	Intraoperative fluids: 2000 mL of crystalloid	Nutritional supplementation	Regular paracetamol	Morphine for breakthrough			Provision of hospital contact numbers, review on ward if problems within 2 wk
Faiz *et al*[16]	Functional assessment and goal setting Stoma nurse Bowel preparation in left-sided resections	Minimal-access surgery Local anaesthetic infiltration to the largest wound No drains or NG tubes	Patient sat out in chair	3 high-protein/ high-calorie drink Normal diet offered Patient sat out in chair Start walking Removal of urinary catheter for colonic resections Laxatives				Review in outpatient clinic on day 12
Jottard *et al*[7]	Nutrition supplementation Functional assessment and goal setting No bowel preparation	Thoracic epidural Standard anesthetic protocol Prevention of intraoperative hypothermia No drains or NG tubes	Free fluid	All IV fluid stopped Normal diet offered				Use of anti-emetics Early mobilization Postoperative nutritional care
Maessen *et al*[20,21]	Nutrition supplementation[1]	Thoracic epidural	Oral analgesia	All IV fluid stopped	Removal of epidural Removal of urinary catheter			
Nygren *et al*[22]	Functional assessment and goal setting	Prevention of intraoperative hypothermia	Patient sat out in chair	Nutritional supplements > 400 mL				
Hendry *et al*[23]	No bowel preparation	Transverse/ curved incision	Nutritional supplements Free fluid > 800 mL	Normal diet offered Patient sat out in chair				

Soop *et al*[26]	Nutrition supplementation	Thoracic epidural	Prophylactic antiemetics	Regular paracetamol and NSAIDS Patient sat out in chair	Patient sat out in chair	Patient sat out in chair	Epidural removed (at least)	
Raymond *et al*[28]	Nutrition supplementation Functional assessment and goal setting	Thoracic epidural Intra-operative targeted fluid management No NG tube						Early mobilization/ resumption of diet
Turunen *et al*[10]	Functional assessment and goal setting	Thoracic epidural		Removal of urinary catheter				Early mobilization/ resumption of diet
	Preoperative feeding	High-oxygen P						No routine opioids, regular paracetamol and NSAIDS
	Bowel preparation	Prevention of hypothermia No drains or NG tubes						Fluid restriction
Senagore *et al*[35]		No NG tube	PCA Free fluids	Removal of urinary catheter Normal diet offered regular NSAIDs, gabapentin, hydroxycodone if needed No drains				
Wennstrom *et al*[11]	Functional assessment and goal setting No bowel preparation Preoperative oral hydration	Thoracic epidural Short acting anaesthetics No opioids	Free fluid Patient sat out in chair		Epidural removed Urinary catheter removal			
Mohn *et al*[18]	Nutrition supplementation Functional assessment and goal setting Bowel preparation	Thoracic epidural Total intravenous anaesthesia Intra-operative targeted fluid management Prophylactic antiemetics Short midline incisions No drains or NG tubes	Patient sat out in chair	Removal of urinary catheter Patient sat out in chair Normal diet offered Regular paracetamol and NSAIDs, opioids for breakthrough	Epidural removed			Regular laxatives twice daily Restricted postoperative intravenous fluids
Teeuwen *et al*[17]	Nutrition supplementation Bowel preparation in left-sided resections	Thoracic epidural Transverse incisions except in Crohn's disease and rectal surgery Intra-operative targeted fluid management (hypotension treated with vasopressors) Prophylactic antiemetics No drains or NG tubes	Free fluids Nutritional supplements Patient sat out in chair	Normal diet offered Intravenous fluid administration Start walking	Epidural removed Urinary catheter removal Regular Paracetamol NSAIDs, opioids for breakthrough			
Ahmed *et al*[24,25]	Nutrition supplementation Functional assessment and goal setting No bowel preparation	High inspired oxygen Concentration Transverse incisions No drains or NG tubes	Free fluids Soft diet offered Patient sat out in chair	Start walking				Regular paracetamol NSAIDs, opioids for breakthrough

Kirdak *et al*[19]	Nutrition supplementation	Thoracic epidural	Start walking	NG tubes and urinary catheters removed (except pelvic dissection)	Removal urinary catheter (low pelvic operations) and drains	Epidural removed
	Bowel preparation	Pelvic drains with rectal dissections		Soft diet offered		Regular paracetamol
		Urinary, central venous, and nasogastric catheters were routinely used		Patient sat out in chair		Central venous catheters removed
				Start walking		Normal diet

[1]These authors followed Kearon for the nutritional supplementation. NBM: Nihil by mouth; NG: Nasogastric; IV: Intravenous; NSAIDs: Non-steroidal antinflammatory drugs; PCA: Patient-controlled analgesia.

Table 2 Clinical characteristics of studies examined

Ref.	Type of study	Patients (*n*)	Sex (males%)	Age (yr)	Type of surgery	Approach	Length of stay (d)	Morbidity	Mortality	Readmission	Comments
King *et al*[14]	Prospective case series	60	31 (52)	72 ± 11		ERAS	5.8	11 (18%)	2 (3%)	7 (12%)	ERAS ↓ hospital stay
		86	45 (52)	70 ± 11		Conventional	10.7 ($P < 0.001$)	24 (28%)	6 (7%)	8 (9%)	
Maessen *et al*[20]	Observational study	425	-	-	Resections above peritoneal reflection	ERAS	5 d	-	-	-	Delay in discharge was due to the development of major complications
Maessen *et al*[21]	Case series	121	67 (55)	66 ± 12	Resections above peritoneal reflection without stoma	ERAS	Discharge delay = 1 d	-	-	-	↓ in hospital stay may relate to changes in organization of care and not to a shorter recovery period
		52	22 (42)	64 ± 12	Resections above peritoneal reflection without stoma	Conventional	Discharge delay = 2 d				
Jottard *et al*[7]	Prospective ERAS group matched with historical data	36	-	-		ERAS	6 (3-27)	-	-	-	ERAS was implemented in a district general hospital
		92	-	-		Conventional	9 (3-64)	-	-	-	
Hendry *et al*[23]	Prospective case series	1035	498 (48.10)	59 (69-78)		ERAS	6 (4-8)	294 (28.40%)	17 (1.60%)	86 (8.60%)	Higher ASA, advanced age, sex (male) and rectal surgery associated with delayed mobilization, morbidity and prolonged stay
Mohn *et al*[18]	Prospective ERAS group matched with historical data	94	40 (43)	66		ERAS		29 (31%)	1 (1%)	14 (15%)	ERAS ↓ hospital stay
		153	68 (44.40)	71 (15-90)		Conventional	11 (5-108)	27 (18%)	1 (1%)	-	
Nygren *et al*[22]	Prospective ERAS group matched with historical data	99	-	-		ERAS	-	18%[1]	-	15%[1]	ERAS ↓ time to resumption of oral diet, mobilization and passage of stool, improved lung function, ↓ morbidity and hospital stay but ↑ readmissions
		69	27	65 ± 2		Conventional	8.6 ± 0.6/7 for colonic resection 12.7 ± 1.2/11 for rectal resection	17 (37%) for colonic 12 (52%) for rectal resection	0	2 (4%) for colonic 1 (4%) for rectal	

Ahmed *et al*[24]	Retrospective case series	231	101 (44)	68 (56-76)	Elective open bowel resection	ERAS	6 (5-9)		-	-	Lower ASA grade, use of epidurals and avoidance of regular oral opiates are associated with an earlier discharge
Kahokehr[9]	Prospective case series	100	-	68 (31-92)		ERAS	4 (3-46)	-	-	-	Lower ASA score, transverse incision laparotomy and laparoscopy associated with earlier discharge
Teeuwen *et al*[17]	Prospective ERAS group matched with historical data	61	22 (36.1)	57 ± 17.6	elective open colonic or rectal resection	ERAS	6 (3- 50)	9 (14.8%)	0%	2 (3.3%)	ERAS ↓ morbidity and hospital stay
		122	-	-		Conventional	9 (3-138)	33.60%	1.60%	1.60%	
Bryans *et al*[34]	Retrospective case series	20	-	-	Colorectal surgery with stoma (excluding abdominoperineal resection)	ERAS	mean = 7	-	-	-	ERAS ↓ hospital stay and ability to manage stoma
		20				Conventional	mean = 20				
Kahokehr *et al*[8]	Prospective case series	74	-	-	Open right hemicolectomy	ERAS	Median (43-28)	-	-	-	No difference in morbidity or surgical recovery
		39			Laparoscopic right hemicolectomy	Conventional	5 (2-18)				

[1]Significant difference. ERAS: Enhanced recovery; ASA: American society of anesthesiologists score; QOL: Quality of life.

median hospital stay was 4-6 d compared to 8-9 d following CC[7,9,17,20,27,28]. There was no evidence that the relative effect of ERAS on LOS varied according to the type of surgery (laparoscopic, laparoscopic converted, open)[14]. In one study ERAS reduced the LOS equally in both laparoscopic (from a median of 7 d to a median of 5 d) and open surgery (from a median of 9 d to a median of 7 d)[28]. However, there was no change or improvement in the time taken to return to full activity for either group[28].

Significant predictors for longer discharges using ERAS protocols are the patient's fitness for surgery [American society of anesthesiologists (ASA) score greater than 1][9,20,23,24], higher physiological and operative severity score for the enumeration of mortality and morbidity scores[20], the use of oral opiates in the postoperative period[24], age[20,23,24], rectal surgery[23], complex resections[20], the development of major complications[20] and the inability to discharge patients when they had reached functional recovery[20]. In fact, the increase in LOS with age might be attributed to delayed discharge related to difficulties in arranging social care (see below). Contrasting results were reported for the postoperative duration of epidurals [24,29] and the use of a transverse *vs* midline incision[9,24], sex[9,23].

The readmission rate after ERAS is 3%-15% and is similar to CC[14,17,23,24]. Only Nygren showed a significant higher readmission rates after ERAS (4% *vs* 15 %)[22].

Mortality and morbidity

Most studies found no significant differences in mortality rates between ERAS and CC which ranged between 1.6% and 2% [17,18,22,23,27]. The overall morbidity rate after ERAS is 18%-28% (anastomotic leak 2%-5%, reoperation rate 7.4%)[23,24] (Table 2). Morbidity rates were lower than those published for the same units before the introduction of an ERAS protocol (35%)[27]. However, contrasting results were reported by other articles. Some studies showed similar overall complication rates[14,17,22] for both colonic and rectal resections[22], others claimed lower morbidity rates after ERAS (14.8% *vs* 33.6%)[17], others higher rates with ERAS but only for minor complications (nausea, wound infection)[18]. Morbidity was predicted by ASA grade Ⅲ–Ⅳ, male sex and rectal surgery[30], while low BMI or advanced age were not associated with it[23].

FUTURE CHALLENGES

Laparoscopic vs open resection on ERAS

Randomized trials involving the application of ERAS protocols to laparoscopic surgery showed conflicting results[12,31] (Table 3). A recent review of the published literature suggests that little additional benefit is added by laparoscopy to an already well-established ERAS program[32] especially in terms of postoperative quality of life[13], but a large multicentre study is still ongoing[33]. Patients who underwent laparoscopic surgery had a shorter LOS than those having open surgery (4-6 d for the laparoscopic group *vs* 6-10 d for the open group) for both colonic and rectal surgery[12,16]. Readmission rates also were lower after laparoscopic surgery (5.8%

Table 3 Other colorectal studies involving enhanced recovery after surgery patients

Ref.	Type of study	Patients (*n*)	Approach	Comments
Soop *et al*[26]	RCT	9 *vs* 9	Complete or hypocaloric postoperative enteral nutrition on ERAS	Complete enteral nutritions was associated with minimal postop insulin resistance, hyperglycemia and nitrogen losses
King *et al*[12]	RCT	43 *vs* 19	Lap *vs* open resections on ERAS patients	Reduced hospital stay and with laparoscopic resections
King *et al*[13]	RCT	41 *vs* 19	Lap *vs* open resections on ERAS patients	Laparoscopic surgery achieves quicker return to daily activities
Kirdak *et al*[19]	RCT	14 *vs* 13	Preop. dexamethasone *vs* placebo on ERAS patients	Preoperative dexamethasone has no significant effects on the inflammatory response or outcomes
Turunen *et al*[10]	RCT	29 *vs* 29	Epidural anesthesia *vs* control for laparoscopic resection on ERAS	The epidural G. needed less oxycodone than the control G. Until 12 h postop. Epidural alleviated pain, reduced opioids requirements
Raymond *et al*[28]	Retrospective case series	179 *vs* 144	Lap *vs* open resections on ERAS patients	Laparoscopic surgery achieves quicker return to daily activities
Blazeby *et al*[15]	Prospective	20	Laparoscopic assisted and open	QOL evaluation. Patients liked quicker discharges, few were dissatisfied due to complications requiring readmissions
Senagore *et al*[35]	RCT	22 *vs* 21 *vs* 21	Standard *vs* lactated Ringer's *vs* hetastarch-lactated Ringer's periop fluid	Individualized intraoperative fluid management with crystalloid reduced overall fluid administration compared to colloid
Faiz *et al*[16]	Prospective non-randomized	191 *vs* 50	Lap *vs* open resections on ERAS patients	Laparoscopic has advantages over open approach also in ERAS patients
Wennstrom *et al*[11]	Prospective	32	ERAS	Postoperative survey on QOL following discharge: fatigue, nausea and bowel disturbances
Ahmed *et al*[25]	Case series	100 *vs* 95	ERAS audit protocols application *vs* ERAS clinical practice	Observance to ERAS protocol was lower outside clinical trials

RCT: Randomized controlled trial; ERAS: Enhanced recovery after surgery; QOL: Quality of life; Preop.: Preoperative; Postop.: Postoperative.

vs 22.0%)[16]. No significant differences were found in the overall morbidity (52% after laparoscopic *vs* 42% after open surgery) and major morbidity (15% after laparoscopic *vs* 26% after open surgery)[8,12,16] while contrasting results were reported for mortality rates: one study showed no significant differences[12] while another claimed higher mortality after open surgery[16]. Differently, Basse *et al*[31] did not reveal significant differences in LOS or morbidity between groups, but these authors excluded patients with rectal anastomoses (requiring a stoma) and those not living independently at home that required social setting for discharge. In fact, the social discharge is a problem that was also faced by Kahokehr and colleagues in their study (see below)[8].

Functional recovery and delay in discharge

In the pre-ERAS era 90% of patients were not discharged on the day that criteria were fulfilled. Wound care and symptoms pointing towards an anastomotic leakage were the most important reasons for a medical appropriate delay of discharge[21]. With regards for the stoma independence, 60% of patients audited in the pre-ERAS era were taking more than 8 d to be deemed stoma-independent and only 15% were able in less than 5 d. Following the introduction of ERAS protocols the percentage of patients not discharged on the day that criteria were fulfilled decreased to 34%-87%[20,21], 75% of patients achieved stoma independence in 5 d or less and only 5% took 8 or more days - the figures completely reversed compared to the pre-ERAS era[34]. Results achieved represent a huge step forward especially considering that they simply reflect an optimization of the patients' management and of the impact of surgery without the necessity to introduce any additional procedures into clinical practice. At the same time they also show us that 13%-66% of patients are still not discharged when deemed medically fit by one or two days[24]. Various authors feel that ERAS protocols ultimately optimized the patient's medical fitness for discharge and that nowadays a further reduction of the LOS must relate to changes in the organization of care and not to shorter recovery periods. This could be obtained in example by evidencing those social factors that can delay the discharge and therefore organizing the available resources outside the hospitals well in advance the operation. In example, older patients leaving alone and likely requiring specialist assistance or short admissions to nursing homes or rehabilitative structures can be individuated during the preoperative counseling and necessary arrangements well planned before surgery.

When asked about their experience with the ERAS programs, most patients appreciated a planned short hospital stay because it was perceived that better recovery could be achieved in the home environment[15] (Table 3). However, some of them reported feeling vulnerable at home so shortly after major surgery and those who experienced complications were less satisfied with the process[15]. The first period at home is the most troublesome and the main problems perceived are fatigue, nausea and bowel disturbances (not pain)[11] (Table 3). In this view, it is necessary that ERAS programs are paralleled by the development of services aimed to provide

direct contacts and accesses to healthcare resources that could reassure patients about their recovery when normal or quickly individuate suspicious symptoms that require readmissions[8,15]. A direct telephone contact is a simple measure that might alleviate the patient anxiety and maintain the continuity of care from health professionals[11].

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