

Prospective Study of Role of Multimodal Perioperative Management Protocol in Colorectal Cancer Surgery

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ABSTRACT

Introduction: Patients undergoing colorectal surgery often face prolonged hospital stays and increased complication rates. This study aimed to evaluate the effectiveness of a multimodal perioperative management protocol in reducing hospital stay, complications, 30-day readmission rates, and mortality in patients undergoing elective colorectal cancer surgery.

Methods: This prospective randomized controlled trial included 30 patients admitted for surgery after confirmed diagnosis and randomized into multimodal (n=14) and control (n=16) groups. The multimodal group received specialized perioperative care, while the control group received standard care. Statistical analyses employed unpaired t-tests at a confidence interval of 95% ($p < 0.05$).

Results: The multimodal group exhibited significant improvements in various postoperative parameters compared to the control group. Notably, there were reduced durations for post-op mobilization (1.0 vs. 1.68 days, $p = 0.003$), bowel sounds (1.92 vs. 2.64 days, $p = 0.001$), and oral feeding tolerance (2.21 vs. 3.06 days, $p = 0.021$). Hospital stay was notably reduced in the multimodal group (6.64 days) compared to the control group (8.25 days, $p = 0.002$). Additionally, complications were significantly lower in the multimodal group (13.40%) compared to the control group (20.31%, $p = 0.019$), as were 30-day readmission rates (14.28% vs. 25%, $p = 0.029$). Mortality rates were also reduced in the multimodal group (7.14%) compared to the control group (12.5%).

Conclusion: Implementation of a multimodal perioperative management protocol significantly reduced hospital stays, complications, readmission rates, and mortality in patients undergoing colorectal cancer surgery compared to standard care.

Key Word- Colorectal cancer, perioperative, multimodal, ERAS, Colorectal surgery

INTRODUCTION

Patients undergoing colorectal surgery, where resection of bowel is involved, can have a complication rate of between 15% and 20% [1–3]. Such complications can prolong postoperative hospital stay by 6 to 10 days [4]. The financial burden imposed on health care systems due to prolonged hospital stay after colorectal surgery can be significant. In an effort to reduce the length of hospital stay after colorectal surgery, Kehlet et al. [5] were the first to describe in detail a specific protocol called “fast-track” or “enhanced recovery after surgery” protocol which had the potential to reduce hospital stay to a mean of 4 days. Many protocols have been put forward by hospital groups which consist of varying individual preoperative, intraoperative, and postoperative fast-track elements such as preoperative counselling and feeding, no bowel preparation, perioperative high oxygen concentrations, active prevention of hypothermia, no routine use of nasogastric tubes and drains [6–14]. Wind et al. [15] conducted a metanalysis of six studies (three RCTs and three CCTs) with a total of 512 patients which showed a reduction in primary hospital stay and morbidity for patients in fast-track programs after elective colorectal surgery. However, in 2000, Basse and Kehlet described a clinical pathway to accelerate recovery after colonic resection which dramatically cut down length of stay. Their study described a median stay of 2 days with a readmission rate of 15% [16-17]. The aim of our study is to attenuate the surgical stress response, accelerate recovery, decrease complications, minimize hospital stay, readmission rate and mortality.

PATIENT AND METHODOLOGY

This was a prospective randomized controlled study. Patients who were undergoing elective colorectal cancer surgery in our hospital over the course of one year were included as subjects of the study. Sample size was calculated to be 30 in both multimodal and control groups. The study was powered 80% ($\alpha = 0.05$, $\beta = 0.80$) to assuming the difference in mean duration of nasogastric tube removal and early feeding to be 1.1 days and $SD = 1$ in multimodal and control group.

Randomization of patients was done by Simple block randomization method. Continuous data was analysed by unpaired t-test in multimodal and control group. Continuous data was expressed in the form of proportion or percentage. Continuous data was expressed in mean ± SD. The trend of continuous data was kept at 95% confidence interval (p value=<0.05).

This prospective randomized controlled trial enrolled patients undergoing elective colorectal cancer surgery at our institution. Patients meeting inclusion criteria were randomized into multimodal and control groups using the Simple block method. The multimodal group received specialized perioperative care, including intravenous fluid restriction, prokinetic agents for oral intake, early ambulation, nasogastric tube removal, enteral feeding, and preoperative antibiotic prophylaxis. The control group received standard care. Statistical analyses employed unpaired t-tests at a confidence interval of 95% (p<0.05) to compare outcomes between the two groups.

OBSERVATION AND RESULTS

1. Post operative parameters distribution in study groups. (Table 1)

SNo.	Post op parameters	Multimodal group(n=14) Mean(2SD) days	Control group (n=16) Mean(2SD) days	P value
1	NG removal	1.35(1.99)	2.06(1.54)	0.038
2	Post op mobilization	1.0(0.78)	1.68(1.40)	0.003
3	Bowel sounds	1.92(0.95)	2.64(1.20)	0.001
4	Flatus	2.42(1.02)	3.31(1.40)	0.001
5	Motion	2.78(1.78)	4.0(2.42)	0.004
6	Oral feeding	2.21(1.73)	3.06(2.07)	0.021
7	Normal /solid diet	3.85(1.32)	4.81(2.09)	0.007
8	Urine catheterization	2.71(1.22)	3.37(2.05)	0.044
9	Fluid restriction	2.42(1.09)	3.65(1.07)	0.001
10	Hospital stay	6.64(1.68)	8.25(3.04)	0.002

*NG-nasogastric tube,op-operative,n=number of patients,SD=standard deviation,SNo.-serial number

(Table 1)

2. Postoperative complications distribution in study groups (Table 1)

S No.	complications	Multimodal group (n=14)						Control group(n=16)						P value
		AR n=4		APR n=4		Hemi colectomy n=6		AR n=4		APR n=6		Hemi colectomy n=6		
		n	%	n	%	n	%	n	%	n	%	n	%	
1	Wound infection	1	25	1	25	1	16.67	1	25	2	33.33	2	33.33	0.019
2	Anastomotic leak	1	25	0	0	0	0	1	25	0	0	1	16.67	
3	Urinary /sexual dysfunction	0	0	2	50	0	0	1	25	3	50	0	0	

4	Stoma complication	0	0	1	25	0	0	0	0	2	33.33	0	0
5	Chest infection	1	25	0	0	1	16.67	2	50	1	16.67	1	16.67
6	Cardiac	1	25	1	25	0	0	2	50	1	16.67	0	0
7	PONV	1	25	0	0	2	33.33	2	50	1	16.67	1	16.67
8	Mortality	1	25	0	0	0	0	1	25	0	0	1	16.67

*PONV-post operative nausea and vomiting, AR-anterior resection, APR-abdominal perineal resection, %-percentages

(Table 1)

3. Comparison of multimodal perioperative protocol in various Randomized control studies (Table 3)

Study	Preoperative counselling	Bowel preparation	Preoperative Feeding	Fluid restriction	Minimal invasive incision	NG removal	No use of drain	Post operative mobilization	Post operative feeding	urine catheter	Systemic use of morphine	Antibiotic prophylaxis
Anderson ADG et al (2003)	+	-	+	-	+	+	+	+	+	-	-	+
Delney CP et al(2003)	+	+	-	+	-	+	-	+	+	+	+	-
Gatt M et al(2005)	+	-	+	-	+	+	+	+	+	-	-	+
KhooCK et al(2007)	+	+	-	-	-	+	-	+	+	-	-	-
Present study	+	+	+	+	+	+	-	+	+	+	-	+

(Table 3)

4. Comparison of results of various Randomized control studies (Table 4)

Study	Year	Design	No. of patients (n)		Hospital stay(days) Mean(2SD)		Mortality %		Readmission %	
			MG (n)	CG (n)	MG	CG	MG	CG	MG	CG
Anderson ADG[6]	2003	RCT	14	11	4 (1.8)	7(2.1)	0	9	0	0
Delney CP[8]	2003	RCT	31	33	5.4 (2.5)	7.1 (4.8)	-	-	10	18

<i>Gatt M[10]</i>	2005	RCT	19	20	6.6 (4.4)	9 (4.6)	5	0	5	20
<i>Khoo CK[13]</i>	2007	RCT	35	35	5 (8.5)	7 (14.35)	0	6	9	3
<i>Present</i>	2017	RCT	14	16	6.64 (1.68)	8.25 (3.04)	7.14	12.5	14.28	25

*MG-multimodal group, CG-control group, RCT-randomized control trial

(Table 4)

CONCLUSION

In our study mean duration of bowel sounds (1.92+/-0.95 vs.2.64+/-1.20), motion (2.78+/-1.78 vs.4.0+/-2.42) and tolerance to normal diet (3.85+/-1.32 vs.4.81+/-2.09) days found significantly in multimodal and control group respectively which is concordance with Arenal JJ et al [1] concluded bowel movements (1.7±0.89 vs. 3.27±1.3), defecation (3.4±0.77 vs. 4.38±1.18) and time of tolerance of solid diet (2.48±0.85 vs. 4.77±1.81). Mean duration of nasogastric removal (1.35+/-1.99 vs.2.06+/-1.54),flatus (2.42+/-1.02 vs.3.31+/-1.40) days observed significantly in study groups which is comparable with Reissman et al [24] concluded the early and regularfeeding groups in the rate of vomiting (21% vs. 14%), nasogastric tube reinsertion (11% vs. 10%), length of ileus (3.8 +/- 0.1 days vs. 4.1 +/- 0.1 days), early feeding (2.21+/-1.73 vs. 3.06+/-2.07) days which resemble with Anderson et al [6]. concluded that patients in the optimization group tolerated a regular hospital diet significantly earlier than controls (48 versus 76 h; P < 0.001). Hospital stay noticed (6.64+/-1.68 vs.8.25+/-3.04) days which show concordance with Anderson ADG et al [6] concluded (4+/-1.8 vs 7+/-2.1d, P = 0.002) Delaney CP et al [8] (5.4 vs. 7.1 days; P = 0.02) Gatt M et al, [10] (6.6 +/-4.4 vs 9 +/-4.6d, P = 0.027) Khoo CK et al,[13] (5 vs. 7 days; P < 0.001) Yang et al, [18] (6.0 ± 1.0 vs 11.7 ± 3.8 d, P < 0.001) maximum hospitalization found in Khoo CK et al [13] and minimum in Anderson ADG et al [6]. Mean duration of catheterization (2.71+/-1.22 vs.3.37+/-2.05) which concordance with Gatt M et al [10] who concluded that duration of catheterization (P = 0.022) significant. Mean intravenous fluid restriction (2.42+/-1.22 vs.3.37+/-2.05) litres comparable with. Mackay et al [21] concluded that the median total intravenous fluid intake in the restricted group was 4.50 (4.00-5.62) litres compared with 8.75 (8.00-9.80) litres in the standard group (P < 0.001) overall

complication in our study (13.40% vs.20.31% $p=0.0019$) in multimodal and control group respectively which show concordance with Brandstrup et al [22] concluded that The restricted intravenous fluid regimen significantly reduced postoperative complications both by intention-to-treat (33% versus 51%, $P = 0.013$) and per-protocol (30% versus 56%, $P = 0.003$) analyses. The numbers of both cardiopulmonary (7% versus 24%, $P = 0.007$) and tissue-healing complications (16% versus 31%, $P = 0.04$) were significantly reduced. Noblett et al [26] concluded that major postoperative complications (2 versus 15 per cent; $P = 0.043$).

In our series readmission rate is calculated (14.28 vs 25% $p =0.029$) which comparable with Christensen et al [20] concluded the readmission rate was 15% in the fast-track group and 16% with the control patients. Gustafsson et al [23] concluded readmissions was significantly reduced with increasing adherence to the ERAS protocol (>90%) compared with low ERAS adherence (<50%). In our study mortality recorded 7.5% in multimodal and 12.5% in control group significantly which is concordance with Anderson ADG et al,[6] (0% vs9%), Gatt M et al,[10] (5% vs 0%), Khoo CK et al,[13] (0% vs 6%) respectively.

Conclusion

Enhanced recovery programs is shown to be effective in reducing overall hospital stay and readmission without compromising patient safety or increasing morbidity. There is good evidence that multimodal management protocol form the mainstay of elective colorectal surgery.

Bibliography

1. Arenal, J. J., Benito, C., Concejo, M. P., & Ortega, E. Colorectal resection and primary anastomosis in patients aged 70 and older: prospective study. *The European Journal of Surgery = Acta Chirurgica*, (1999). 165(6), 593–7. <https://doi.org/10.1080/110241599750006523>
2. Bokey, E. L., Chapuis, P. H., Fung, C., Hughes, W. J., Koorey, S. G., Brewer, D., & Newland, R. C. Postoperative morbidity and mortality following resection of the colon and rectum for cancer. *Dis Colon Rectum*, (1995). 38(5), 480–487. <https://doi.org/10.1007/BF02148847>

3. Retchin, S. M. Perioperative management of colon cancer under Medicare risk programs. *Archives of Internal Medicine*,(1997).157(16), 1878–1884.
<https://doi.org/10.1001/archinte.157.16.1878>
4. Basse PH, Whiteside TL, Herberman RB Use of activated natural killer cells for tumor immunotherapy in mouse and human. *Methods Mol Biol*(2000), 121:81–94
5. Kehlet H, Mogensen T Hospital stay of 2 days after open sigmoidectomy with a multimodal rehabilitation programme. *Br JSurg*(1999) ,86(2):227–230
6. Anderson AD, McNaught CE, MacFie J, Tring I, Barker P, Mitchell CJRandomized clinical trial of multimodal optimization and standard perioperative surgical care. *Br J Surg* (2003) ,90(12):1497–1504
<https://doi.org/10.1002/bjs.4371>
7. Basse L, Raskov HH, Hjort Jakobsen D, Sonne E, Billesbolle P, Hendel HW, Rosenberg J, Kehlet H Accelerated postoperative recovery programme after colonic resection improves physical performance, pulmonary function and body composition.*Br J Surg* (2002), 89(4):446–453
8. Delaney, C. P., Zutshi, M., Senagore, A. J., Remzi, F. H., Hammel, J., & Fazio, V. W. (2003). Prospective, randomized,controlled trial between a pathway of controlled rehabilitation with early ambulation and diet and traditional postoperative care after laparotomy and intestinal resection. *Diseases of the Colon and Rectum*, 46(7), 851–859.
<https://doi.org/10.1007/s10350-004-6672-4>
9. Fearon, K. C. H., Ljungqvist, O., Von Meyenfeldt, M., Revhaug, A., Dejong, C. H. C., Lassen, Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clinical Nutrition (Edinburgh, Scotland)*, (2005). 24(3), 466–77.
<https://doi.org/10.1016/j.clnu.2005.02.002>
10. Gatt M, Anderson AD, Reddy BS, Hayward-Sampson P, Tring IC,MacFie J Randomized clinical trial of multimodal optimization of surgical care in

patients undergoing major colonic resection. *Br J Surg* (2005) , 92(11):1354–1362 <https://doi.org/10.1002/bjs.5187>

11. Jakobsen DH, Sonne E, Andreasen J, Kehlet H Convalescence after colonic surgery with fast-track vs conventional care. *Colorectal Dis*(2006) , 8(8):683–687
12. Kehlet H Fast-track colonic surgery: status and perspectives. *Recent Results Cancer Res*(2005), 165:8–13
13. Khoo, C. K., Vickery, C. J., Forsyth, N., Vinall, N. S., & Eyre-Brook, I. A. (2007). A prospective randomized controlled trial of multimodal perioperative management protocol in patients undergoing elective colorectal resection for cancer. *Annals of Surgery*, 245(6), 867–72. <https://doi.org/10.1097/01.sla.0000259219.08209.36>
14. Polle SW, Wind J, Fuhling JW, Hofland J, Gouma DJ, Bemelman WA Implementation of a fast-track perioperative care program: what are the difficulties? *Dig Surg* (2007) ,24(6):441–449
15. Wind J, Polle SW, Fung Kon Jin PH, Dejong CH, von Meyenfeldt MF, Ubbink DT, Gouma DJ, Bemelman W Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg* (2006) , 93(7):800–809
16. Basse L, Hjort Jakobsen D, Billesbolle P, et al. A clinical pathway to accelerate recovery after colonic resection. *Ann Surg.*(2000),232:51–57.
17. Kehlet H, Mogensen T. Hospital stay of 2 days after open sigmoidectomy with a multimodal rehabilitation programme. *Br J Surg.*(1999),86:227–230
18. Yang, D. J., Zhang, S., He, W. L., Huang, W. Q., Cai, S. R., Chen, C. Q., ... Zhan, W. H. Fast-track surgery accelerates the recovery of postoperative humoral immune function in elective operation for colorectal carcinoma: a randomized controlled clinical trial. *National Medical Journal of China*, (2012), 92(16), 1112–1115. <https://doi.org/http://dx.doi.org/10.3760/cma.j.issn.0376-2491.2012.16.009>
19. Andersen, J., Hjort-Jakobsen, D., Christiansen, P. S., & Kehlet, H. Readmission rates after a planned hospital stay of 2 versus 3 days in fast-track

- colonic surgery. *British Journal of Surgery*, (2007), 94(7), 890–893
<https://doi.org/10.1002/bjs.5669>
20. Christensen, H. K., Thaysen, H. V., Rodt, S. Å., Carlsson, P., & Laurberg, S. Short hospital stay and low complication rate are possible with a fully implemented fast-track model after elective colonic surgery. *European Surgical Research*, (2011) 46(3), 156-161.
<https://doi.org/10.1159/000324406>
21. MacKay, G., Fearon, K., McConnachie, A., Serpell, M. G., Molloy, R. G., & O'Dwyer, P. J. Randomized clinical trial of the effect of postoperative intravenous fluid restriction on recovery after elective colorectal surgery. *The British Journal of Surgery*, (2006), 93(12), 1469–74.
<https://doi.org/10.1002/bjs.559>
22. Brandstrup, B., Tønnesen, H., Beier-Holgersen, R., Hjortsø, E., Ørding, H., Lindorff-Larsen, K., ... Pott, F. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Annals of Surgery*, (2003), 238(5), 641–8. <https://doi.org/10.1097/01.sla.0000094387.50865.23>
23. Gustafsson, U. O., Hausel, J., Thorell, A., Ljungqvist, O., Soop, M., Nygren, J., & Enhanced Recovery After Surgery Study, G. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Archives of Surgery*, (2011). 146(5), 571–577.
<https://doi.org/10.1001/archsurg.2010.309>
24. Reissman, P., Teoh, T. A., Cohen, S. M., Weiss, E. G., Nogueras, J. J., & Wexner, S. D. Is early oral feeding safe after elective colorectal surgery? A prospective randomized trial. *Ann Surg*, (1995). 222(1), 73–77.
<http://www.ncbi.nlm.nih.gov/pubmed/7618972>
25. Guenaga, K. F., Matos, D., Castro, A. A., Atallah, A. N., & Wille-Jorgensen, P. Mechanical bowel preparation for elective colorectal surgery. *Cochrane Database Syst Rev*, (2005), (1), CD001544.s
<https://doi.org/10.1002/14651858.CD001544.pub2>
26. Noblett, S. E., Snowden, C. P., Shenton, B. K., & Horgan, A. F. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. *British Journal of Surgery*, (2006), 93(9), 1069–1076. <https://doi.org/10.1002/bjs.5454>

