Original article

Accelerated postoperative recovery programme after colonic resection improves physical performance, pulmonary function and body composition

L. Basse, H. H. Raskov†, D. Hjort Jakobsen, E. Sonne†, P. Billesbølle, H. W. Hendel*, J. Rosenberg and H. Kehlet

Departments of Gastroenterology and *Clinical Physiology and Nuclear Medicine, Hvidovre University Hospital, Hvidovre and †Department of Surgical Gastroenterology, Copenhagen University Hospital, Gentofte, Denmark
Correspondence to: Dr H. Kehlet, Department of Gastroenterology 435, Hvidovre University Hospital, DK-2650 Hvidovre, Denmark
(e-mail: henrik.kehlet@hh.hosp.dk)

Background: **Postoperative organ dysfunction contributes to morbidity, hospital stay and convalescence. Multimodal rehabilitation with epidural analgesia, early oral feeding, mobilization and laxative use after colonic resection has reduced ileus and hospital stay.**

Methods: **Fourteen patients receiving conventional care (group 1) and 14 patients who had multimodal rehabilitation (group 2) were studied before and 8 days after colonic resection. Outcome measures included postoperative mobilization, body composition by whole-body dual X-ray absorptiometry, cardiovascular response to treadmill exercise, pulmonary function and nocturnal oxygen saturation.**

Results: **Defaecation occurred earlier (median day 1 *versus* day 4) and hospital stay was shorter (median 2 *versus* 12 days) in patients who had multimodal treatment. Lean body and fat mass decreased in group 1 but not in group 2. Exercise performance decreased by 44 per cent in group 1 but was unchanged in group 2. A postoperative increase in heart rate (HR) response to exercise was avoided in group 2. Pulmonary function decreased in group 1 but not in group 2. There was less nocturnal postoperative hypoxaemia in group 2. Cardiac demand–supply (HR/oxygen saturation ratio) increased in group 1 but not in group 2.**

Conclusion: **Multimodal rehabilitation prevents reduction in lean body mass, pulmonary function, oxygenation and cardiovascular response to exercise after colonic surgery.**

Paper accepted 3 December 2001

British Journal of Surgery 2002, **89**, 446–453

Introduction

Colonic and other major surgical procedures are associated with postoperative pain, paralytic ileus, reduced pulmonary function and loss of muscle mass and function[1], all of which may contribute to postoperative morbidity and need for hospital stay. It was shown previously in a descriptive study that a multimodal rehabilitation programme, including continuous epidural analgesia, early oral nutrition, enforced mobilization, and cisapride and laxative use, reduced ileus and postoperative hospital stay to 2–3 days after colonic resection[2].

The aim of the present study was to assess the changes in postoperative organ function in patients undergoing colonic resection with multimodal rehabilitation and to compare the results with those of patients receiving conventional care.

Patients and methods

The study was prospective, controlled and non-randomized. Fourteen consecutive patients from the Department of Surgical Gastroenterology, Copenhagen University Hospital, Gentofte received conventional care (group 1) and 14 consecutive patients from the Department of Gastroenterology, Hvidovre University Hospital, Hvidovre received multimodal rehabilitation (group 2) after elective open right hemicolectomy or sigmoid colon resection. Exclusion criteria were age less than 18 years, patients with pacemaker or other implanted metal, patients requiring a stoma or an anastomosis less than 12 cm from

The Editors have satisfied themselves that all authors have contributed significantly to this publication

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Table 1 Protocol for anaesthesia, surgery and rehabilitation programme after colonic resection with conventional care (group 1) and multimodal rehabilitation (group 2)

	Conventional care (group 1)	Multimodal rehabilitation (group 2)
Anaesthesia	Premedication: oral diazepam 10 mg Epidural catheter T8–T10 Carbocaine 2% 4 + 4 ml with adrenaline Carbocaine 2% 4 ml with adrenaline hourly General anaesthesia Fentanyl 0·1 mg Thiomebumal 3–5 mg/kg Rocuronium Oxygen–nitrous oxide–sevoflurane Dextran 70 (Macrodex®) 500 ml Saline 3000 ml (maximum)	No premedication Epidural catheter Right hemicolectomy T6–T7 Sigmoid resection T9–T10 Test: lignocaine 2% 3 ml with adrenaline Bupivacaine 0·5% 6 + 6 ml Bupivacaine 0·25% 5 ml 2 hourly at operation Morphine 2 mg if < 70 years old Morphine 1 mg if ⩾ 70 years old General anaesthesia Remifentanil 1 μg per kg per min Propofol 2–4 mg per kg per h Cisatracium 0·15 mg/kg Hydroxyethyl starch (HAES®) 500 ml Saline 1500 ml (maximum) Ondansetron 4 mg Ketorolac 30 mg Bupivacaine 0·25% 20 ml (incision)
Surgery	Median laparotomy	Transverse or curved incision[2]
After operation	Continuous epidural analgesia (3 days) Bupivacaine 0·25% 4 ml/h Morphine 0·2 mg/h Breakthrough pain Intramuscular or intravenous morphine After removal of epidural catheter Morphine 10 mg orally on request No standard care programme; fluid, food, mobilization and discharge depending on the attending surgeon Postoperative nasogastric tube depending on surgeon who performed the operation	Continuous epidural analgesia (2 days) Bupivacaine 0·25% 4 ml/h Morphine 0·2 mg/h Breakthrough pain Ibuprofen 600 mg orally Bupivacaine 0·12% 6 ml epidurally Morphine 10 mg orally (last choice) Food, protein drink approximately 60–80 g protein per day and mobilization from the day of surgery following a well defined nursing care programme[2] Day of surgery start Acetaminophen (slow release) 2 g 12 hourly Magnesia 1 g 12 hourly Cisapride 20 mg 12 hourly First day after operation Remove bladder catheter in the morning Second day after operation Remove epidural catheter in the morning Discharge after lunch

the anus, and patients unable to perform the preoperative test programme. The local ethics committee approved the study and informed patient consent was obtained before investigation according to the Helsinki II declaration.

The perioperative care programme is detailed in *Table 1*. Mobilization (hours out of bed per day) was assessed daily by the patient during the first week after operation by means of a questionnaire.

Pulmonary function (forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and peak expiratory flow (PEF)) was measured with a vitalograph (Micro Plus Spirometer MS03; Micro Medical, Rochester, UK) before operation and 6 h, 24 h, 48 h and 8 days after surgery with the patient in the sitting position.

Body composition (lean body mass (LBM), fat mass (FM) and weight) was measured before and 8 days after surgery by whole-body dual X-ray absorptiometry (DXA)[3,4] (XR 36 DXA scanner™; Nordland, Fort Atkinson, Illinois, USA) with the patient in a supine position wearing light clothing without shoes, 2 h after a light breakfast and voiding. The scanner was calibrated before scanning. All scans were performed in Hvidovre University Hospital by L.B. and H.W.H. DXA parameters were obtained from measurements on femur. Body-weight was also measured on hospital scales (Liebra; N. C. Nielsen, Copenhagen, Denmark).

The cardiovascular response to treadmill exercise was assessed until exhaustion or the heart rate (HR) reached 120

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Table 2 Demographics of patients undergoing colonic resection with conventional care (group 1) or multimodal rehabilitation (group 2)

	Conventional care (group 1; *n* = 14)	Multimodal rehabilitation (Group 2; *n* = 14)
Age (years)	64 (52–79)	74 (33–94)
Weight (kg)	70 (55–137)	72 (42–105)
Height (cm)	171 (157–185)	166 (143–175)
ASA		
I	4	1
II	7	6
III	3	7
Type of surgery		
Right hemicolectomy	5	10
Sigmoid resection	9	4
Preoperative haemoglobin (mmol/l)	7·8 (5·7–9·1)	7·5 (5·0–9·4)
Blood loss (ml)	225 (100–2000)	200 (0–1000)
0–24 h intravenous fluid (ml)	3750 (3000–5500)	3325 (2150–4000)*

Values are median (range). ASA, American Society of Anesthesiologists. *$P < 0{\cdot}05$ *versus* conventional care (Mann–Whitney *U* test)

per min, before operation and 8 days after surgery. The tests were performed on an electronic treadmill (J 502; Tunturi®, Piispanristi, Finland). The start speed was adjusted according to body-weight; a 1° increase in elevation corresponded to a 5-W workload increase. The patient walked for 3 min at each workload to reach steady state. After each 3-min period the HR was measured and the treadmill was elevated. The workload and energy performed were calculated as described previously[5]. All tests were performed in Hvidovre University Hospital by L.B. and D.H.J.

Oxygen saturation (constant hypoxaemia: mean saturation (SpO_2), duration of SpO_2 below 90 per cent; episodic hypoxaemia: number of episodes in which the oxygen saturation dropped 5 per cent or more for at least 10 s within 2 min) and HR were measured continuously during one night before surgery and during the first two nights after surgery (23.00 hours to 07.00 hours) by pulse oximetry (Nellcor N-3000 L™ Nellcor Puritan Bennett, Pleasanton, California, USA). Oxygen saturation data were downloaded to a computer (Score Software version 1.0C 1997; Nellcor).

Mental function was assessed before operation and 24 h, 48 h and 8 days after surgery by the Hodkinson[6] modification of the original Roth–Hopkins test[7], which consisted of 26 questions that tested short- and long-term memory, recognition, orientation and cognitive function.

Pain at rest and during movement from the supine to the sitting position was scored every 4 h (except at night) for the first 2 days after operation, daily in the morning from postoperative day 2 to 7 and weekly for a total of 4 weeks using a scale from 0 to 3 (0, no pain; 1, slight pain; 2, moderate pain; 3, severe pain). Nausea and fatigue were scored using a similar scale and at the same intervals during the first and fourth weeks after operation. The area under the curve (AUC) for each variable was calculated and used for statistical evaluation.

Serum albumin and plasma C-reactive protein (CRP) were analysed before operation and on day 8 after surgery.

Data are presented as median (range). Comparisons were done using the Mann–Whitney and Wilcoxon signed rank tests. Friedman two-way analysis of variance was used to compare differences for repeated data within groups. $P \leqslant 0{\cdot}05$ was considered statistically significant.

Results

Demographic data are shown in *Table 2*. There were no significant differences between groups, except for a smaller volume of perioperative intravenous fluids in group 2. Postoperative defaecation occurred on day 4 (2–7) in group 1 and on day 1 (0–2) in group 2 ($P < 0{\cdot}001$). Postoperative hospital stay was 12 (5–21) days in group 1 and 2 (2–4) days in group 2 ($P = 0{\cdot}001$).

Mobilization

The total time out of bed during the first postoperative week was 87 (64–121) h in group 2 and 61 (19–84) h in group 1 ($P < 0{\cdot}01$) (*Fig. 1*).

Body composition

Perioperative changes in total body-weight within each group and between the groups were insignificant. LBM on the femur decreased significantly in group 1 by 429 g (7 per cent) ($P < 0{\cdot}05$), but increased insignificantly by 158 g (2

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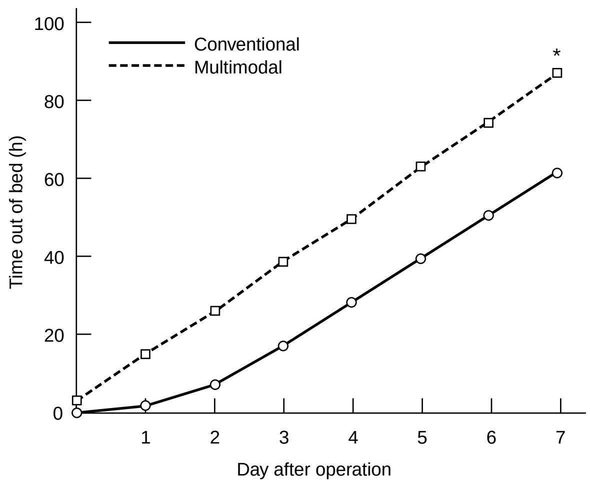

Fig. 1 Mobilization during the first week after elective colonic resection in patients who had conventional care (group 1) and multimodal rehabilitation (group 2). $^{*}P < 0{\cdot}05$ *versus* conventional care (Mann–Whitney test)

per cent) in group 2 (*Fig. 2*) ($P < 0{\cdot}05$ between groups) (Mann–Whitney test). FM on the femur decreased significantly in group 1 by 329 g (6 per cent) ($P < 0{\cdot}05$), but insignificantly by 77 g (1 per cent) in group 2 (*Fig. 2*) ($P > 0{\cdot}05$ between groups) (Mann–Whitney test).

Treadmill exercise

Before operation two patients in group 1 and five patients in group 2 were exhausted before reaching a HR of 120 per min, compared with eight patients in group 1 and six patients in group 2 after operation. *Fig. 3* shows the amount of work performed in the two groups before and after operation until exhaustion or with the HR at 120 per min. The amount of work performed decreased significantly by 44 per cent in group 1 ($P < 0{\cdot}05$) and insignificantly by 12 per cent in group 2 ($P < 0{\cdot}05$ between groups). The work performed per increase in HR decreased significantly by 0·33 W per heartbeat (27 per cent) in group 1 during the first postoperative week ($P < 0{\cdot}05$), but insignificantly by 0·08 W per heartbeat (8 per cent) in group 2.

Oxygen saturation

Median SpO_2 decreased on the second postoperative night in group 1 ($P < 0{\cdot}05$), but not in group 2 (*Table 3*). The time spent with an SpO_2 below 90 per cent was higher on the second postoperative night than before operation in group 1 ($P < 0{\cdot}05$), but no change occurred in group 2. The number of hypoxaemic episodes in the two groups was no different ($P > 0{\cdot}05$), although there were more episodes of hypoxaemia on the second night after operation in group 2 (*Table 3*). HR changes within and between groups were not significant (*Table 3*). The postoperative change in HR/SpO_2 ratio, as an indicator of the cardiac demand (HR)–supply (oxygen) balance is shown in *Fig. 4*. The HR/SpO_2 ratio increased significantly in group 1 ($P < 0{\cdot}05$), but was unchanged in group 2.

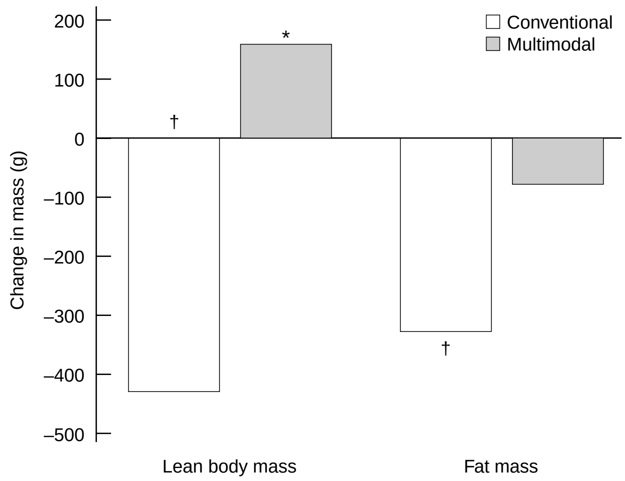

Fig. 2 Change in femoral lean body mass and fat mass from before operation to 1 week after colonic resection in patients who had conventional care (group 1) and multimodal rehabilitation (group 2). $^{*}P < 0{\cdot}05$ *versus* conventional care (Mann–Whitney test), $^{\dagger}P < 0{\cdot}05$ from before operation to 8 days after surgery in conventional care group (Wilcoxon)

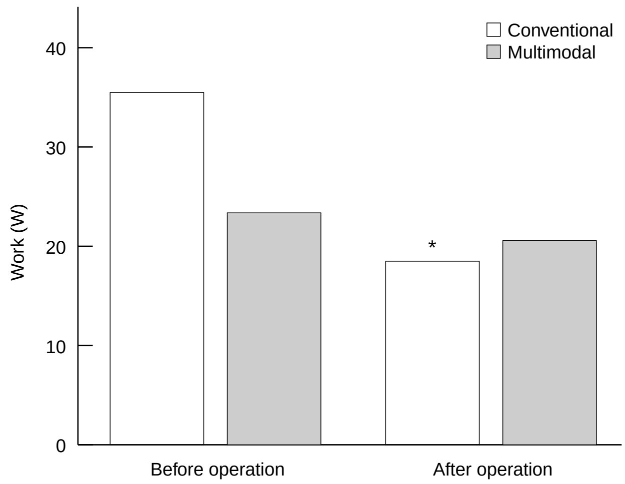

Fig. 3 Amount of work performed until exhaustion or heart rate reached 120 per min before and 1 week after colonic resection in patients who had conventional care (group 1) and multimodal rehabilitation (group 2). The decrease in amount of work performed was significantly different between groups ($P < 0{\cdot}05$). $^{*}P < 0{\cdot}05$ *versus* before operation in conventional care group (Mann–Whitney test)

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Table 3 Median oxygen saturation, constant hypoxaemia, episodic hypoxaemia and heart rate before operation and during the first two nights after surgery (23.00 to 07.00 hours) in patients undergoing colonic resection with conventional care (group 1) or multimodal rehabilitation (group 2)

	Conventional care (group 1; *n* = 14)	Multimodal rehabilitation (Group 2; *n* = 14)
Median Spo_2 (%)		
Before operation	96 (94–99)	95 (89–97)
1st postop. night	95 (92–98)	95 (90–98)
2nd postop. night	93 (86–97)*	94 (88–98)
$Spo_2 \leq 90\%$ (min)		
Before operation	0 (0–12)	0 (0–257)
1st postop. night	0 (0–44)	0 (0–260)
2nd postop. night	58 (0–402)*	0 (0–322)
Desaturation (events ≥ 10 s)		
Before operation	2 (0–139)	4 (0–175)
1st postop. night	3 (0–380)	0 (0–138)
2nd postop. night	21 (0–274)	3 (0–102)
Heart rate (per min)		
Before operation	69 (57–95)	76 (51–102)
1st postop. night	75 (54–101)	76 (59–98)
2nd postop. night	77 (56–109)	74 (58–102)

Values are median (range). Spo_2, oxygen saturation; postop., after operation. *$P < 0.05$ *versus* before operation in conventional group (Wilcoxon test). There were no differences between groups before operation

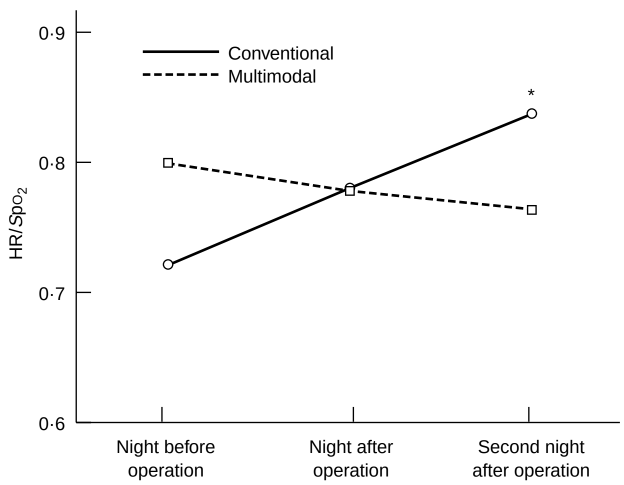

Fig. 4 Change in heart rate (HR)/oxygen saturation (Spo_2) ratio in the early postoperative period, measured during one night before surgery and during the first two nights after operation (23.00 hours to 07.00 hours) in patients who had conventional care (group 1) and multimodal rehabilitation (group 2). *$P < 0.05$ *versus* before operation in conventional care group (Mann–Whitney test)

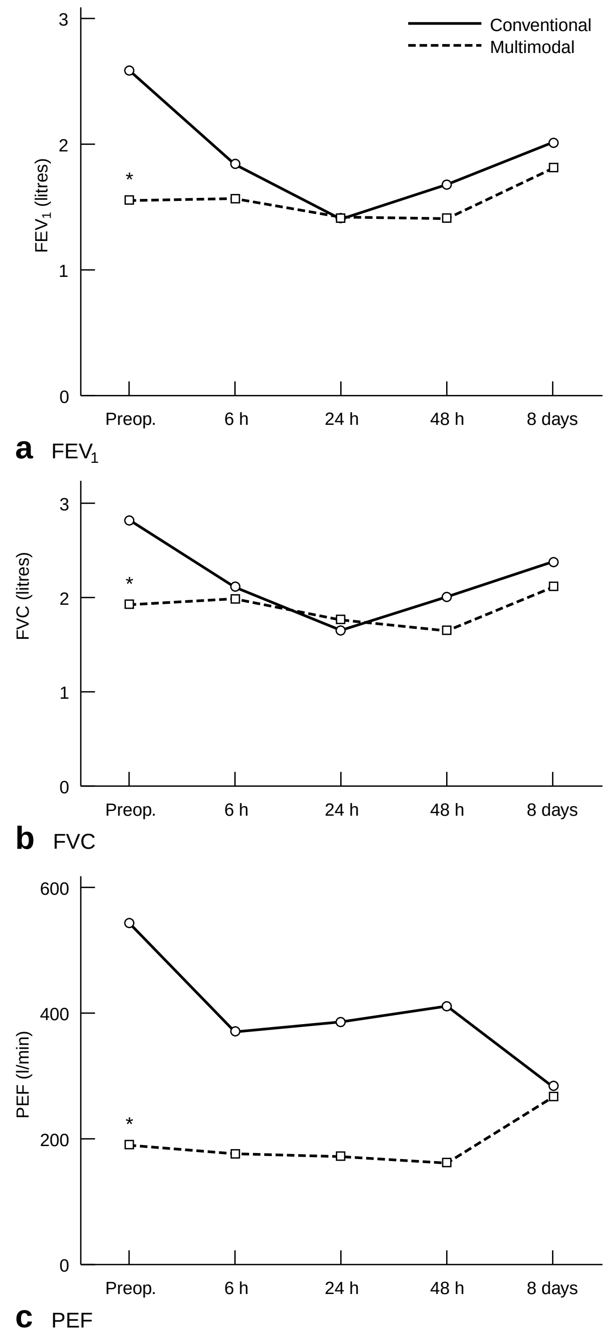

Fig. 5 Changes in pulmonary function during the early period after colonic resection in patients who had conventional care (group 1) and multimodal rehabilitation (group 2). **a** Forced expiratory volume in 1 s (FEV_1), **b** forced vital capacity (FVC) and **c** peak expiratory flow (PEF). FEV_1, FVC and PEF were impaired during the perioperative period in group 1 ($P < 0.05$). *$P < 0.05$ between groups before operation

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Pulmonary function

Before operation patients in group 1 had significantly better pulmonary function (FEV_1, FVC and PEF) than those in group 2 ($P < 0{\cdot}05$). Patients in group 1 experienced impairment in pulmonary function during the first week after operation ($P < 0{\cdot}05$). In contrast, there was no change in pulmonary function during the first postoperative week in group 2 (*Fig. 5*).

Mental test

There were no perioperative differences within or between groups in mental test scores.

Pain, fatigue and nausea

Group 1 had significantly more pain (AUC 30) at rest during the first 2 days after operation than group 2 (AUC 10) ($P < 0{\cdot}05$), but no differences in pain between the groups were observed during mobilization, in fatigue during the first 30 days or in nausea during the first postoperative week.

Serum albumin and plasma C-reactive protein

Median serum albumin level decreased significantly from 572 to 513 µmol/l in group 1 ($P < 0{\cdot}01$), but insignificantly from 538 to 502 µmol/l in group 2. Median plasma CRP concentration increased from below 95 to 122 nmol/l in group 1 and from 103 to 203 nmol/l in group 2 during the first postoperative week (*P* not significant).

Morbidity and readmissions

In group 1 one patient had a postoperative wound infection and dehiscence, one patient had postoperative ileus and required treatment with a nasogastric tube for 4 days, and one patient was readmitted for nausea and social reasons on day 22. In group 2 one patient was readmitted on day 14 with mechanical bowel obstruction, one patient was readmitted for 1 day on day 13 because of a urinary tract infection, and one patient was treated in the outpatient clinic for a wound infection.

Discussion

The results of this prospective non-randomized study showed that the usual postoperative organ dysfunction (ileus, pulmonary dysfunction, catabolism and decreased work performance) did not occur after colonic resection with multimodal rehabilitation compared with conventional postoperative care. These results have important clinical implications because postoperative organ dysfunction contributes to morbidity and length of hospital stay[1].

It may be argued that the study should have been randomized, but it was impossible to randomize and blind patients and nurses to multimodal rehabilitation or conventional care in the same ward. When the necessary cultural changes involved in a multimodal rehabilitation programme[1] have been introduced it is difficult, if not unethical, to randomize patients to traditional care with no specific attention towards early mobilization and oral nutrition, since these care principles have been proven to be valid[1]. Furthermore, revised care practices, including avoidance of gastrointestinal tubes, drains and prolonged urinary catheterization, are impossible to randomize in a ward where care has already been adjusted to a fast-track programme[1].

The improved early active mobilization with more hours out of bed during the first postoperative week in patients with multimodal rehabilitation may have contributed to several positive outcomes including improved pulmonary function and oxygen saturation[8], and less reduction of postoperative LBM and work performance[9]. The institution of early enforced postoperative mobilization requires an optimized pain relief programme, in which continuous epidural analgesia with a mixture of local anaesthetic and low-dose opioid is most effective[10]. Another important factor is patient education, and the introduction of the well defined nurse care programme in which daily requirements for mobilization are followed[2]. Interestingly, both study groups received continuous epidural postoperative analgesia, but pain was less in the group that had active rehabilitation during the first 2 days. The explanation for this may be the reduced duration of postoperative ileus associated with less discomfort and pain, facilitated by epidural analgesia, early nutrition and laxative use.

The demonstrated improvement in pulmonary function may have important clinical implications in reducing pulmonary morbidity, as shown in an earlier study of 100 consecutive patients (including high-risk patients) undergoing colonic resection without pulmonary morbidity[2,11]. Although epidural analgesia *per se* may improve pulmonary function and outcome[12], the combination of continuous epidural analgesia with enforced early mobilization may represent a further means of improving pulmonary outcome. The improved oxygen saturation brought about by early mobilization[8] may secondarily have important clinical implications by reducing postoperative cardiac morbidity, cerebral dysfunction and wound complications[13]. Multimodal rehabilitation may have important effects on cardiac morbidity since the HR/SpO_2 ratio is reduced, reflecting a more favourable cardiac energy supply–demand balance. Further data are required to document such

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potential advantages, but previous experience of 100 consecutive patients with a median age of 73 years has demonstrated a very low (less than 3 per cent) wound and cardiac morbidity rate[2,11].

The observed reduction in postoperative loss of LBM and work performance may be a consequence of several factors associated with multimodal rehabilitation. Even a short period of immobilization will lead to muscle atrophy, negative nitrogen balance and loss of LBM[9]. Also, early oral nutrition with protein drinks may have facilitated preservation of LBM. The preservation of LBM and work performance may have important implications for elderly patients undergoing major surgery, since such patients already have a decreased physiological reserve capacity[14] which may increase the risk of postoperative morbidity. The femur was used to assess changes in LBM and FM by DXA since fluid retention after abdominal surgery occurs mainly in the trunk[15]. In contrast, a large part of the muscle mass is localized on the femur and thus may represent the 'true' LBM compared with 'total' LBM in the postoperative state.

The physiological response to exercise decreased after operation in patients undergoing conventional rehabilitation as demonstrated previously[16]. This change did not occur in patients undergoing multimodal rehabilitation, even though these patients were older and less fit before operation. However, the patients who had multimodal rehabilitation had been home for a median of 6 (range 4–6) days compared with the continued hospitalization in the conventional care group, and the documented increased mobilization may therefore have preserved physical performance.

Another feature of the multimodal rehabilitation programme is the reduction in paralytic ileus from 3–5 days to 1–2 days[2]. The pathogenesis of postoperative ileus is multifactorial[10], but continuous epidural analgesia with local anaesthesia has been shown to reduce ileus[10,17]. Early oral feeding, mobilization and use of laxatives may also have contributed, although the relative role of these factors has not been established from randomized controlled trials[17]. The reduction of ileus may facilitate early oral feeding, which otherwise has been shown to improve physical performance and LBM[18,19], while even short-term starvation decreases work capacity[20].

The present small and non-randomized study provides substantial evidence in support of the hypothesis that aggressive postoperative rehabilitation is superior to conventional postoperative care. The findings should serve as a stimulus to further investigation of the concept of multimodal postoperative rehabilitation and to the initiation of large multicentre comparative studies.

Acknowledgements

This work was supported by a grant from Apotekerfonden 1991 (L.B. and D.H.J.) and the Danish Research Council 9902757 (H.K.).

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Dual publication

Readers may care to review the following two articles: 'Blankensteijn JD, Lindenburg FP, van der Graaf Y, Eikelboom BC. Influence of study design on reported mortality and morbidity rates after abdominal aortic aneurysm repair. *Br J Surg* 1998; **85:** 1624–30' and 'Blankensteijn JD. Mortality and morbidity rates after conventional abdominal aortic aneurysm repair. *Semin Interv Cardiol* 2000; **5:** 7–13'.

The Editors find a remarkable similarity in the text and tables of these articles; data shown in the later paper are the same as those shown in Figure 1 of the *BJS* paper. While the *BJS* article is referenced in the bibliography of the later paper, there is no acknowledgement of the previous 1998 publication. Our publishers, Blackwell Publishing Limited, have no record of any communication with either Dr Blankensteijn or the publishers of *Seminars in Interventional Cardiology*, Harcourt Publishers Limited.

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