Quality assurance in rectal cancer treatment

Dulk, M. den

Chapter 10

Improved diagnosis and treatment of anastomotic leakage after colorectal surgery

Marcel den Dulk, Saidja L. Noter, Eduard R. Hendriks, Mark A.M. Brouwers, Cornelis H. van der Vlies, Rob J. Oostenbroek, Anand G. Menon, Willem-Hans Steup, Cornelis J.H. van de Velde

Eur J Surg Oncol 2009; 35: 420-426.

ABSTRACT

Aim

This study aimed at testing feasibility of a standardised postoperative surveillance protocol to reduce delay in the diagnosis of anastomotic leakage (AL) and, subsequently, mortality.

Material and methods

Patient files of patients operated between 1996 and 1999 were reviewed and used as historical controls (n = 1066). As a result, a protocol for standardised postoperative surveillance was designed using easily accessible, clinical parameters. Between August 2004 and August 2006, all operated patients with a colorectal anastomosis (n = 223) were prospectively subjected to this standardised surveillance.

Results

AL was diagnosed in 7.0% of patients in the historical control group and 9.4% of patients in the standardised surveillance group. AL mortality decreased from 39% to 24% with standardised surveillance (n.s.). The delay in AL diagnosis was significantly reduced during standardised surveillance (4 versus 1.5 days, P = 0.01), which was confirmed in the multivariate analysis.

Conclusion

With non-standardised postoperative monitoring, AL was associated with a high mortality rate. Patients were subjected to several additional tests, which were not primarily useful to diagnose AL. Standardised postoperative surveillance for AL was introduced successfully and resulted in a shorter delay between the first signs and symptoms to the confirmation of AL.

INTRODUCTION

Anastomotic leakage (AL) is a feared complication after colorectal surgery causing morbidity and mortality.[1] Different percentages are published for the incidence of AL, varying between 1 and 25%, partly depending on the method of evaluation and the level of the anastomosis.[2-5] AL does not only result in increased and serious morbidity and mortality,[6-9] but has also been associated with a higher local recurrence rate after curative treatment of colorectal malignancies.[10,11]

In literature, different mortality rates after AL are reported.[8,12,13] In the evaluation of surgery, slowly, more attention is focussed on adverse events such as postoperative morbidity and mortality.[14] AL can never be reduced to zero and therefore it is of relevant importance to control the negative and sometimes fatal sequelae in case an AL occurs. Consequently, not only the occurrence but also the clinical outcome after AL might be considered as a performance indicator of surgical care. Firstly, this study aimed at investigating the occurrence of AL and associated mortality in several training hospitals in the Netherlands. Secondly, we hypothesised that the interval between first signs or symptoms and action on AL can influence the clinical outcome. As a result, a standardised postoperative surveillance protocol was designed which aimed at reducing the delay in the diagnosis of AL and subsequently at reducing the mortality rate. The feasibility of this surveillance protocol was studied prospectively.

PATIENTS AND METHODS

Retrospective analysis

Patient files from all patients of three training hospitals (Haga Hospital location Leyenburg (The Hague), Haga Hospital location Red Cross (The Hague) and Albert Schweitzer Hospital (Dordrecht)) in whom a colorectal anastomosis was created were reviewed (part of the data previously published[15] and presented at the Surgical Infection Society Meeting in 2003[16]). As AL is an issue after both resections for malignant and benign diseases, we included all resections in this period in the study. Malignancies were colon or rectal cancer, whereas benign diseases included resections for polyps, ulcerative colitis, diverticulosis, Crohn's disease, and continuity restoration after a stoma. Delay in the diagnosis of AL was calculated as the period from the first signs of clinical deterioration to confirmation of the diagnosis. These signs consisted of the presence of fever (temperature >38.0°C), ileus (absence of passage of faeces or air after the third postoperative day) or an elevated number of leukocytes in the blood count (>12.0 x 10^9/l).

Design of the protocol for standardised postoperative surveillance for AL

The results of the retrospective study led to the design of a protocol for standardised postoperative monitoring aiming to reduce the delay in the diagnosis of AL and subsequently to reduce AL related mortality. Literature was used to select postoperative variables which are prognostic for AL. Furthermore, the items had to be easily available during normal patient visits. The final selection process was done by MdD, MB and WS and are shown in Table 1. The items related to laboratory tests were checked at least every other day. For each item, points were given as shown in Table 1. If an item was scored as normal or if an item was not scored (such as items related to laboratory investigation), no points were given, whereas if the item was scored as abnormal, 1 or 2 points were given. The weight of an abnormal score was depending on the diagnostic importance of that specific item (determined by MdD, MB and WS). The sum of all items gave a score: the leakage-score. In case of more than one score determined within 24 h, the worst score was used.

Table 1. Items scored in the prospective study.

Item	Normal value	Score (points)	Abnormal value	Score (points)
General				
Fever	≤ 38.0°C	0	> 38.0°C	1
Heart rate	≤ 100/min	0	> 100/min	1
Respiratory rate	≤ 30/min	0	> 30/min	1
Urinary production	≥ 30 ml/h or 700 ml/day	0	< 30 ml/h or 700 ml/day	1
Mental status	Normal mental status	0	Agitation or lethargic	2
Clinical condition	Stable or improving condition	0	Deterioration	2
Local physical examination				
Signs of ileus	No ileus	0	Ileus	2
Gastric retention	No gastric retention	0	Gastric retention	2
Fascial dehiscence	No fascial dehiscence	0	Fascial dehiscence	2
Abdominal pain, other than wound pain	No pain other than wound pain	0	Pain other than wound pain	2
Laboratory investigation				
Signs of infection	No increase in leukocyte number or CRP	0	Increase of ≥ 5% in leukocyte number or CRP	1
Kidney function	No increase in urea and creatinine	0	Increase of ≥ 5% in urea or creatinine	1
Diet				
Nutritional status	Normal diet	0	Tube feeding/TPN	1/2

The leakage-score is the sum of all points. If a patient receives both tube feeding and total parental nutrition (TPN), only tube feeding is scored (1 point). CRP = C-reactive protein.

The prospective cohort study

All patients, in whom an intra-abdominal colorectal anastomosis was created in Haga Hospital location Leyenburg from 1 August 2004 to 1 August 2006, were monitored using the standardised postoperative surveillance protocol. Resections were performed both for malignant and benign diseases. Daily, all patients were scored by the treating surgical resident or surgeon (Table 1). The leakage-score was linked to a decision tree indicating the diagnostic and treatment actions that had to be taken (Figure 1). Patients with clinically proven AL (faecal leakage through drains or wounds) bypassed the diagnostic part of the decision tree. Patients were followed until one of the three end-points was reached: AL, postoperative mortality or discharge from the surgical ward. The first symptomatic day of AL was defined as the day after the last day with zero leakage-points before AL was diagnosed. The difference between the first symptomatic day and the day of confirmation of AL was considered to be the delay in the diagnosis of AL.

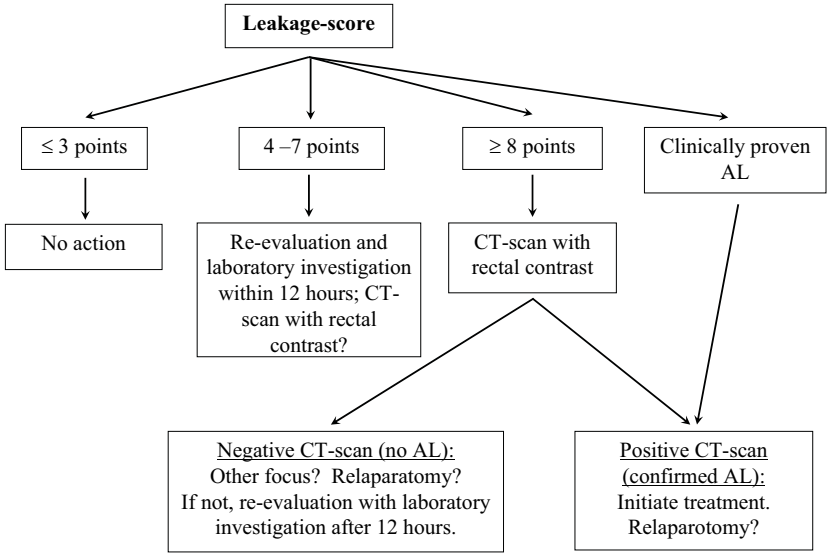

Figure 1. Decision tree of the leakage-score indicating which actions should be taken with each score. Clinically proven anastomotic leakage (AL; faeces in a drain or wound) was treated identically as a positive CT-scan.

Statistical analyses

Data were analysed with the SPSS package (SPSS 14.0 for Windows; SPSS Inc., Chicago, IL). In the analysis for delay, patients from the retrospective analysis were used as historical controls. Univariate analyses with categorical variables were performed with a χ^2 test. Delay and leakage-score were univariately studied using the non-parametric Mann-Whitney test. The multivariate analysis for delay was performed with a ranked ANOVA. A two-sided *P*-value of ≤ 0.05 was considered statistically significant.

RESULTS

Historical controls

In total 1066 resections were performed between 1996 and 1999. Demographic data are shown in Table 2. In this period, 29 patients were treated twice during separate admissions. As these patients were subjected to a risk of AL during each procedure, each admission was considered as a separate patient. AL was diagnosed in 75 patients. Overall mortality was 7.4%. Mortality after the diagnosis AL was 39%.

Before the diagnosis AL was made, several additional diagnostic investigations were performed to exclude other complications such as pneumonia or urosepsis. In 58 of AL patients the following imaging and laboratory studies were performed in the period before confirmation of AL: chest X-ray (*n* = 48), urine sediment test (*n* = 22), ultrasound

Table 2. Demographic data of patients.

Variable	Historical controls	Patients with standardised surveillance
	n = 1066	*n* = 223
Gender		
Male	509	115
Female	557	108
Age		
< 70 years	480	95
≥ 70 years	586	128
Primary disease*		
Malignancy	736	147
Benign disorder	314	76
Timing of procedure		
Elective	906	189
Emergency	160	34
Procedure+		
Right sided resection	391	101
Left sided resection	643	106
Other procedure	32	16
Hospital		
A	335	
B	290	
C	441	223

* Missing for 16 patients; + Right side resection includes ileocecal resection, right sided hemicolectomy, transversectomy, and removal of a stoma in ascending or transverse colon; left sided resection includes left sided hemicolectomy, sigmoid resection, low anterior resection, proctocolectomy, and removal of a stoma in descending colon or sigmoid; other procedure includes subtotal colectomy or unspecified procedures.

investigation (n = 25), CT-scan without contrast enhancement (n = 10), and plain X-ray of the abdomen without contrast (n = 8). In 21, 19 and 18 patients, respectively one, two and more than two of these additional diagnostic tests were used to exclude other complications before AL was diagnosed.

Prospective cohort study with standardised surveillance

In total 224 consecutive resections were performed in the period with standardised postoperative follow-up. During this period 6 patients underwent two resections during separate procedures. One patient was transferred to another hospital and was lost to follow-up and was excluded from all analyses. Demographic details of the remaining 223 patients are shown in Table 2. Twenty-one patients were diagnosed with AL. In total 14 patients died postoperatively. Nine patients died of causes not related to AL: respiratory complications (n = 3), cardio-vascular complications (n = 4), and progression of the malignant disease (n = 2). In all these cases AL was excluded as cause of death. Five patients died after AL was diagnosed.

Leakage-score

The leakage-score was determined daily for every patient. The median score for patients diagnosed with and without AL per day is shown in Figure 2. A significant higher score for patients with AL was found from day 5 to 9. When comparing the median of the highest leakage-score for patients with and without AL, this difference was significant: 7 points (range 0-13) versus 3 points (range 0-10), $P < 0.001$.

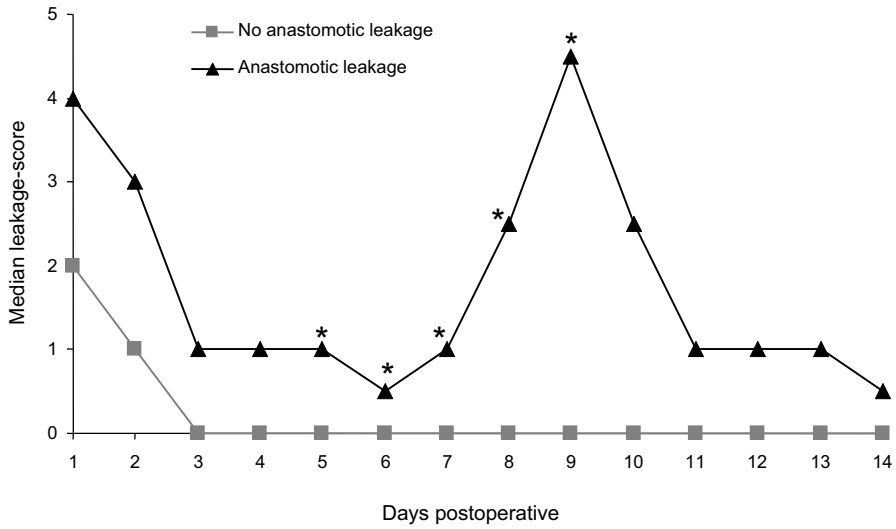

Figure 2. Median scores of patients with and without anastomotic leakage per day. * Indicates a significant difference between patients with and without anastomotic leakage (Mann-Whitney test).

The effects of standardised surveillance on the diagnosis of anastomotic leakage

In the period of standardised surveillance, three patients were dismissed from the hospital without any signs or symptoms on day 6, 7 and 17, respectively. These patients were later readmitted and AL was diagnosed, of whom one patient eventually died. As no information about delay is available for these patients, these patients could not be considered in the analysis for delay. However, these patients were included in all other analyses.

In Table 3 the univariate comparison is shown between patients subjected to standardised monitoring compared with patients without standardised postoperative surveillance. If the three patients who were discarded from the hospital and readmitted before AL was diagnosed were included in the analysis for the day of the diagnosis, no significant difference could be found (median 8 days in the historical control group versus median 6 days after standardised surveillance, $P = 0.22$). However, if these patients were excluded from the analysis, as these patients were not monitored after discharge, the difference was statistically significant (median 8 days versus 6 days, $P = 0.02$). Nevertheless, the delay in the diagnosis of AL was significantly shorter for patients monitored with standardised postoperative surveillance (median 4.0 versus 1.5 days, $P = 0.01$). If the analysis was performed using the same definition of delay in the standardised surveillance group as was used for the historical controls (temperature above 38.0°C, ileus after day 3 or leukocytes blood count >12.0 x 10^9/l), the delay was still significantly shorter (median delay 4.0 days (range 0-21) for historical controls and 3.0 days (range 0-14) after standardised surveillance, $P = 0.03$). In the multivariate analysis, in which patients from both periods are combined, the effects of gender, age, primary disease, timing, procedure, and hospital of treatment were not found to be significantly related to delay (data not shown). Treatment during the period with standardised postoperative surveillance was the only variable that was independently associated with an earlier diagnosis ($P = 0.03$). If for the calculation of delay in the prospective study a cut-off

Table 3. Univariate comparison between controls without standardised postoperative surveillance and patients with standardised surveillance.

	Historical controls	Standardised surveillance	*P*-value
Time to diagnosis since surgery (days)			0.22
Median	8.0	6.0	
Range	1–58	4-47	
Delay in the diagnosis of AL (days)			0.01
Median	4.0	1.5	
Range	0–21	0–21	
Mortality rate of AL diagnosed patients	29/75	5/21	0.21

AL = anastomotic leakage.

point of 4 leakage-points was used instead of 1 point or if the definition of delay as used for the historical controls was used for the group with standardised surveillance, the results were comparable (data not shown). The mortality rate decreased when patients were monitored with standardised surveillance, but this difference was not statistically significant (Table 3).

DISCUSSION

Delay in the diagnosis of anastomotic leakage

AL after colorectal surgery is a frequently occurring, important, postoperative complication, associated with a relatively high mortality rate.[8,9,12,13,17,18] Several studies indicated that delay was associated with increased mortality.[13,19] We studied AL in a retrospective study and developed a protocol for standardised postoperative surveillance, to reduce the delay in the diagnosis and treatment of AL and subsequently to reduce AL associated mortality. AL is found both after malign and benign diseases, although the majority of resections is performed for malignancies. Consequently, a complete cohort of patients was studied, which included both patients with benign and malign diseases, to prevent patient selection. In the present analysis, it is shown that it is feasible to introduce and perform postoperative standardised surveillance for AL after colorectal surgery. This standardised surveillance resulted in a shorter period of delay (median 1.5 day compared to 4 days), independent from gender, age, primary disease, timing of the procedure, type of resection, and hospital of treatment. It should be noted, that it cannot be excluded that the implementation of a standardised postoperative surveillance for AL also increased the awareness of AL, resulting in an earlier diagnosis. However, also in the period 1996-1999 surgeons were familiar with AL. Apparently, awareness of AL alone was insufficient to result in a earlier diagnosis of AL, as it was found not to be easy to notice clinical deterioration in an early stage without the standardised postoperative surveillance protocol.

Mortality after anastomotic leakage

Seven percent of patients treated in the period 1996-1999 were diagnosed with AL, which is in accordance with the percentage reported in literature.[2-5] The observed mortality rate after AL was 39%. Although differences exist in the diagnosis of AL (symptomatic AL versus radiologically proven AL) the highest mortality rate found in literature was reported by the West of Scotland and Highland Anastomosis Study Group.[12] In this study, 40 patients of 1004 had symptomatic AL, of whom 33% died. In general, a mortality rate below 22% is reported in literature.[8,9,13,17,18] In our historical control patients, the relatively large delay could have contributed to the high mortality rate, similar to

findings by others.[13,19] In all patients who died after AL, their death was considered to be related to the AL, which might have resulted in a higher mortality rate than reported in other studies. In the standardised surveillance group five patients died resulting in a decreased mortality rate of 24%, including one patient who died 19 days after the diagnosis of AL due to an aspiration pneumonia and myocardial infarction and one patient who died 125 days after AL due to a palliative treatment setting. Due to this small patient population (n = 5) and differences in the definition of AL mortality, a safe comparison of the mortality rate of the last period with literature can hardly be made.

Variability in diagnostic management

One of the possibilities that might explain the delay in diagnostic management, which was observed in patients treated between 1996 and 1999, is the finding that in 77% of patient various diagnostic procedures were performed to exclude other complications instead of an appropriate diagnostic test for AL, such as a CT-scan with rectal contrast.[20] These additional tests might have resulted in additional delay in the diagnosis of AL. According to the adage "treat first what kills first", exclusion or confirmation of the diagnosis AL (and subsequent treatment) have to take priority in patients with any suspicion of AL after colorectal surgery.

Development of the leakage-score

To reduce variability, a standardised postoperative surveillance protocol was developed which aimed at reducing delay in the diagnosis of AL and subsequently at reducing mortality. Literature was studied to select postoperative variables which have been associated with AL before. In 1991, the Surgical Infection Study Group described the clinical signs of AL which included fever, increased leukocyte count and increased CRP level.[21] Furthermore, Systemic Inflammatory Response Syndrome (SIRS) was indicated to be a sign of AL.[21,22] The following signs could also occur with SIRS: changed mental status, oliguria, increased levels of serum creatinine, and ileus.[23] Finally, the following other postoperative signs were associated with AL: pelvic pain[24], renal failure[13], and peritonitis[25]. Although various groups have described different postoperative parameters that were associated with AL, no scoring system was yet designed nor tested prospectively in a clinical setting. We designed a scoring list, in which most of the above mentioned parameters were included. As no literature was available on the weight of the variables, we determined the weight of the variable based on our opinion of clinical relevance. Most items used to determine the "leakage-score" could be easily obtained during history taking and physical examination, and should normally be recorded daily in the patient's file.

Limits of the analysis

A limit of the present analysis is that prospectively collected data from a single centre are compared with historical controls from three centres. Ideally, a randomised trial is performed, however this is not possible as the investigators will be biased by their knowledge of the protocol when treating a patient in the "conventional" arm. Performing a study in different centres raises the question whether observed differences could be explained just by differences between these centres. If in the present study the analyses were repeated with results from Haga Hospital location Leyenburg only, the results were similar (data not shown). Therefore, the present study using historical data is the best available evidence, although the results should be interpreted with caution.

A difference in the data collection existed between the two periods: retrospective versus prospective. In the historical controls the presence of fever, ileus or an elevated number of leukocytes were considered to be reliably recorded and used in the definition of delay. For comparison, in the prospective study any sign or symptom was considered in the calculation of delay. Therefore, it is likely that signs for anastomotic leakage were detected earlier in the prospective trial, which could have resulted in a relatively longer period of delay in the group followed with standardised surveillance. However, using the definition of delay of the retrospective analysis for the standardised surveillance group still resulted in a significant decrease in delay (median 4 days compared with median 3 days, $P = 0.03$). Apart from that, the period of delay in the historical control group could be underestimated. For this group, patient's files were reviewed, in which the first signs could have been underreported. During a prospective study, this problem is less likely. Due to these differences in data collection the delay could have been underestimated in the historical control group, resulting in an underestimation in the decrease in delay with standardised surveillance.

Further improvements of the leakage-score

In the leakage-score several items were considered. It could however be questioned whether the used cut-off values were chosen optimally. Besides, the present analysis did not study whether all items were weighted properly in the scoring system. Nevertheless, in Figure 2 is shown, that the leakage-score as currently defined, could be used to distinguish the group of patients with and without AL. In order to optimise the leakage-score, a registration project has been launched in several Dutch centres, in which various parameters are collected prospectively for a large number of patients with a colorectal anastomosis in order to come to a more validated scoring system. Eventually, this might result in a modified DUtch LeaKage (DULK) scoring list.

CONCLUSION

AL is a serious complication after colorectal surgery. With non-standardised postoperative monitoring, AL was associated with a high mortality rate. Patients were subjected to several additional tests, which were not useful to diagnose AL. Standardised postoperative surveillance for AL was introduced successfully and resulted in a shorter delay between the first signs and symptoms to the confirmation of AL. In the daily clinical practice, standardised postoperative surveillance after colorectal surgery could be a guide for surgical residents who are developing clinical experience. Its usage could result in improved postoperative care. To further validate the scoring list and decision model, a larger group of patients is necessary. Recently, we started a registration project in several Dutch hospitals. In this project patients are postoperative monitored as normal, without usage of the decision model. Of all patients, various parameters are scored to determine which set of parameters is an early predictor of AL. Eventually, this project will result in an improved and validated DUtch LeaKage scoring list and decision model.

ACKNOWLEDGEMENTS

M. den Dulk is supported by a Quality Assurance Fellowship of the European Society of Surgical Oncology. The authors are grateful to Dr. P.J. Breslau for his help with the collection of the retrospective data and want to thank Professor Dr. T. Wiggers, Dr. H.J.T. Rutten, Dr. P.J. Breslau and E. Meershoek-Klein Kranenbarg for their comments on the draft manuscript.

REFERENCES

1. Hallbook O, Sjodahl R. Anastomotic leakage and functional outcome after anterior resection of the rectum. *Br J Surg* 1996; 83: 60-62.
2. Bokey EL, Chapuis PH, Fung C, Hughes WJ, Koorey SG, Brewer D, et al. Postoperative morbidity and mortality following resection of the colon and rectum for cancer. *Dis Colon Rectum* 1995; 38: 480-486.
3. Matheson NA, McIntosh CA, Krukowski ZH. Continuing experience with single layer appositional anastomosis in the large bowel. *Br J Surg* 1985; 72 Suppl: S104-S106.
4. Merad F, Hay JM, Fingerhut A, Flamant Y, Molkhou JM, Laborde Y. Omentoplasty in the prevention of anastomotic leakage after colonic or rectal resection: a prospective randomized study in 712 patients. French Associations for Surgical Research. *Ann Surg* 1998; 227: 179-186.
5. Tuson JR, Everett WG. A retrospective study of colostomies, leaks and strictures after colorectal anastomosis. *Int J Colorectal Dis* 1990; 5: 44-48.
6. Averbach AM, Chang D, Koslowe P, Sugarbaker PH. Anastomotic leak after double-stapled low colorectal resection. *Dis Colon Rectum* 1996; 39: 780-787.
7. Graf W, Glimelius B, Bergstrom R, Pahlman L. Complications after double and single stapling in rectal surgery. *Eur J Surg* 1991; 157: 543-547.
8. Pakkastie TE, Luukkonen PE, Jarvinen HJ. Anastomotic leakage after anterior resection of the rectum. *Eur J Surg* 1994; 160: 293-297.
9. Rullier E, Laurent C, Garrelon JL, Michel P, Saric J, Parneix M. Risk factors for anastomotic leakage after resection of rectal cancer. *Br J Surg* 1998; 85: 355-358.
10. Bell SW, Walker KG, Rickard MJ, Sinclair G, Dent OF, Chapuis PH, et al. Anastomotic leakage after curative anterior resection results in a higher prevalence of local recurrence. *Br J Surg* 2003; 90: 1261-1266.
11. Petersen S, Freitag M, Hellmich G, Ludwig K. Anastomotic leakage: impact on local recurrence and survival in surgery of colorectal cancer. *Int J Colorectal Dis* 1998; 13: 160-163.
12. West of Scotland and Highland Anastomosis Study Group. Suturing or stapling in gastrointestinal surgery: a prospective randomized study. *Br J Surg* 1991; 78: 337-341.
13. Alves A, Panis Y, Pocard M, Regimbeau JM, Valleur P. Management of anastomotic leakage after nondiverted large bowel resection. *J Am Coll Surg* 1999; 189: 554-559.
14. Obertop H, Gouma DJ. Complications in surgery - let's face them. *Dig Surg* 2002; 19: 83-85.
15. Vrancken Peeters MP, Vrancken Peeters MJ, Corion LU, Breslau PJ. Quality control of colorectal surgery with an extensive complication registration system. *Dig Surg* 2005; 22: 168-173.
16. van der Vlies CH, Gilissen FM, Schnater JM, Hendriks ER, Vrancken Peeters MPFM, Breslau PJ, et al. Colorectal surgery: anastomotic leakage and mortality in three teaching hospitals in the Netherlands (Meeting abstract). *Surgical Infections* 2003; 4: 148.
17. Karanjia ND, Corder AP, Bearn P, Heald RJ. Leakage from stapled low anastomosis after total mesorectal excision for carcinoma of the rectum. *Br J Surg* 1994; 81: 1224-1226.
18. Mealy K, Burke P, Hyland J. Anterior resection without a defunctioning colostomy: questions of safety. *Br J Surg* 1992; 79: 305-307.
19. Macarthur DC, Nixon SJ, Aitken RJ. Avoidable deaths still occur after large bowel surgery. Scottish Audit of Surgical Mortality, Royal College of Surgeons of Edinburgh. *Br J Surg* 1998; 85: 80-83.
20. Eckmann C, Kujath P, Schiedeck TH, Shekarriz H, Bruch HP. Anastomotic leakage following low anterior resection: results of a standardized diagnostic and therapeutic approach. *Int J Colorectal Dis* 2004; 19: 128-133.

21. Peel AL, Taylor EW. Proposed definitions for the audit of postoperative infection: a discussion paper. Surgical Infection Study Group. *Ann R Coll Surg Engl* 1991; 73: 385-388.
22. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med* 1992; 20: 864-874.
23. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003; 31: 1250-1256.
24. Mileski WJ, Joehl RJ, Rege RV, Nahrwold DL. Treatment of anastomotic leakage following low anterior colon resection. *Arch Surg* 1988; 123: 968-971.
25. Nesbakken A, Nygaard K, Lunde OC, Blucher J, Gjertsen O, Dullerud R. Anastomotic leak following mesorectal excision for rectal cancer: true incidence and diagnostic challenges. *Colorectal Dis* 2005; 7: 576-581.