

Risk adjusted benchmarking of clinical anastomotic leakage rate after total mesorectal excision in the context of an improvement project

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Abstract

Aim Anastomotic leakage (AL) after total mesorectal excision (TME) is a major adverse event. This study evaluates variability in AL between centres participating on a voluntary basis in PROCARE, a Belgian improvement project, and how further improvement of the AL rate might be achieved.

Method Between January 2006 and March 2011, detailed data on 1815 patients (mean age 65.5 years, 63% male) who underwent elective TME with colo-anal reconstruction for rectal cancer were registered by 48 centres. Variability in early clinical AL rate was analysed before and after adjustment for gender, age > 60 years, American Society of Anesthesiologists score of 3 or more and body mass index > 25 kg/m².

Results The overall AL rate was 6.7% (95% CI 5.6%–7.9%). Early AL required reoperation in 86.8% of patients. It increased length of hospital stay from 14.7 days to 32.4 days and in-hospital mortality from 1.1% to 4.8%. Statistically significant variability in AL rate between centres was not observed, either before or after risk adjustment. Nonetheless, further improvement may be achievable in

some centres by targeting the adjusted performance of better performing centres. These centres used neoadjuvant treatment, rectal irrigation, mobilization of the splenic flexure, resection of the sigmoid colon, side-to-end colo-anastomosis with or without pouch and defunctioning stoma at primary surgery in a significantly higher proportion of patients than less well performing centres.

Conclusion The overall AL rate was low but needs to be interpreted with caution because of incomplete registration. Further improvement might be achieved by adopting the approach of better performing centres.

Keywords Colorectal surgery, anastomotic leak, rectal cancer, benchmarking, audit

What is new in this paper?

This is the first risk-adjusted benchmarking for anastomotic leakage after total mesorectal excision in centres voluntarily participating in a national improvement initiative. Adjustment was performed for factors that cannot be influenced by the surgeon. Targets were set and surgery-related aspects were identified to improve performance.

Introduction

Advances in the management of rectal cancer have led to improved oncological outcome with a greater proportion of patients undergoing sphincter-preserving operations [1,2]. However, anastomotic leakage (AL), a most feared postoperative complication, frequently requires reoperation(s) resulting in a significant delay of hospital discharge or even mortality [3–6].

The incidence of AL is considered to be an indicator of the quality of care in rectal cancer surgery [7–11]. In view of the potential interference of confounding factors, risk-adjusted analysis is warranted. Multivariable analysis performed in monocentric and multicentric studies based on more than 1000 patients who underwent total or partial mesorectal excision for rectal cancer found the following factors to be independently associated with AL: male gender, age > 60 years, smoking, American Society of Anesthesiologists (ASA) score of 3 or more, neoadjuvant radiotherapy or radiochemotherapy, (ultra)low level of the anastomosis (at the levator level or < 6 cm), intra-operative adverse events, perioperative bleeding and

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absence of a defunctioning stoma [12–17]. The negative effect of neoadjuvant radio(chemo)therapy on the AL rate is controversial. It has not been observed in randomized controlled trials [18–21] nor in a recent German multicentre observational trial [22]. In smaller monocentric studies on low and mid rectal cancer, some other factors have been identified: body mass index (BMI) > 25 or > 30 kg/m² [23,24], pulmonary disease [25], diabetes mellitus [26], coronary heart disease [27], tumour diameter [28], free distal margin < 1 cm [26], operation duration (> 220 min) [29], number of staplers used for laparoscopic rectal division [30], construction of a colon J pouch [25], surgery performed by non-specialized surgeon [26] and no placement of a transanal catheter [26]. In benchmarking for the AL rate after total mesorectal excision (TME) with colo-anal anastomosis, factors that are not controversial and that cannot be influenced by the surgeon should be adjusted for, if available.

National projects aim to improve patient outcome through reduction in the variability between centres. Risk-adjusted variability of the AL rate between centres participating in a national project has not been reported. This study investigates the variability of AL between centres participating in PROCARE, a Belgian multidisciplinary project on cancer of the rectum, based on voluntary participation. It also explores what target setting could be used to strive for an achievable improvement. Surgery-related aspects are compared between centres according to their performance.

Method

Between January 2006 and March 2011, 1912 patients underwent elective TME with colo-anal re-anastomosis for cStage I–IV invasive rectal cancer with its lower limit up to 15 cm above the anal verge. They were registered on a voluntary basis by 79 out of 111 possible hospitals in a dedicated database at the Belgian Cancer Registry (BCR). Thirty-one centres submitted data on fewer than 10 patients (< 5 patients during the whole study period from 21 centres and only a single case from 11 of them), probably related to a lesser degree of commitment to the project. Their results were cumulated and reported separately, but not used for further analysis. In order to allow for more reliable data, analysis was performed after exclusion of patients from these centres, leaving 1815 patients for more detailed analysis. All analyses were performed on anonymized data.

Since participation was on a voluntary basis, completeness of registration by centres that registered a minimum of 10 patients during the study period was assessed through linkage of the BCR, the Intermutualistic

Agency (IMA) database and the PROCARE database. A population-based sample of all rectal cancers (International Classification of Diseases for Oncology, 3rd edition, ICD-O-3 C20) diagnosed in Belgium between 1 January 2006 and 31 December 2008 was available in the BCR. It is mandatory for all pathology laboratories and hospitals to report cases to the BCR. Patients who underwent low anterior resection with TME (code 244042) between 2006 and 2008 were identified in the IMA database. The IMA is an association of the seven Belgian health insurance companies integrating all data related to the medical treatment of all Belgian patients. Health insurance is obligatory for Belgian citizens. The linkage of these data with those of the BCR registry was authorized by the IMA monitoring committee. The merging of data indicated that 34% (607/1766) of patients who underwent low anterior resection with TME between 2006 and 2008 were not registered in PROCARE by the above-mentioned centres during their participation period.

All patients underwent TME with very low anastomosis, i.e. on top of the anal canal (stapled) or in the anal canal (handsewn). AL was defined and graded as proposed by the International Study Group of Rectal Cancer [31]. AL included a defect at the anastomotic site and/or suture and staple lines of neorectal reservoirs, pelvic abscess formation close to the anastomosis and rectovaginal fistula. Only early AL detected during the hospital stay for the primary radical rectal resection and graded B or C are reported in this study. Thus, AL grade A resulting in no change in patient management was not retained for analysis. AL requiring active therapeutic intervention but manageable without re-laparotomy/-scopy was graded B. AL requiring re-laparotomy/-scopy was graded C.

In order to illustrate the overall impact of an AL in this patient cohort, reoperation because of AL, length of hospital stay and in-hospital mortality after primary surgery were compared between patients with and without early AL. Readmissions, e.g. for stoma closure, were not included.

Funnel plots were used to illustrate that the variability in AL between centres exceeded the potential measurement error. The observed AL was plotted against the volume per centre, and prediction limits (e.g. 95% limits) around a specific target outcome (e.g. the overall AL rate) were added. These limits indicate the percentage range of expected AL rates if all centres have the same AL probability. The larger the number of centres is, the smaller the range. Prediction limits were constructed based on a binomial distribution with a continuity correction [32]. Male gender, age (> 60 years), ASA 3 or more and obesity (BMI > 25 kg/m²) were used for

risk-adjusted benchmarking of AL rates. This decision was taken in consensus by members of the PROCARE steering group before analysis. Other factors reported to be independently associated with AL, such as tumour diameter, free distal margin < 1 cm, use of neoadjuvant radio(chemo)therapy, operation duration (> 220 min), intra-operative adverse events, perioperative bleeding, absence of a defunctioning stoma, number of staplers used for laparoscopic rectal division, construction of a colonic J pouch, the use of drains (including transanal drainage), surgical sub-specialization and volume of centres or case-load of surgeons, were not considered 'acceptable' factors for adjustment of the AL rate in the context of a national improvement project with an educational character although most of these factors were available in the database. In view of the equivocal data on neoadjuvant radio(chemo)therapy, it was decided to perform a separate univariate analysis, but not to use radio(chemo)therapy for risk adjustment whatever the result of the analysis.

Statistical analysis

A logistic regression model with a random centre effect was used to test the differences in AL between centres, with and without correction for the above-mentioned risk factors [33,34]. Since many centres had no AL or an AL rate close to zero, a normal distribution for the centre effects was less plausible. Therefore, as a sensitivity analysis, the normal distribution was replaced by an unspecified distribution. The resulting model was estimated with the vertex exchange method algorithm [35], using code written in the R package.

Risk-adjusted AL rates were obtained by multiplying the overall AL rate and the ratio O/E , where O and E refer to the observed and expected number of ALs respectively (after adding a small number in the numerator to handle sampling zeros). The expected number E was obtained from a logistic regression model for AL, with gender (male), age > 60, BMI > 25 and ASA 3 or more as factors for adjustment.

Using χ^2 or Fisher exact tests, it was explored whether tumour- or treatment-related aspects in centres with AL rates above the 50th percentile in the funnel plot differed from those reported by the others.

Results

The overall incidence of early clinical AL in 1912 patients was 6.6% (95% CI 5.5%–7.8%). Fewer than 10 patients were registered by 31/79 centres. Four ALs were reported in the 97 patients (4.1%, 95% CI 1.1%–10.2%) from these 31 centres. After exclusion of these centres,

the overall AL rate in 1815 patients was 6.7% (95% CI 5.6%–7.9%), with no AL observed in 197 patients from 11 out of 48 hospitals. Exclusion of the centres registering fewer than 10 patients had no impact on patient, tumour and surgery-related aspects, except for a non-significant increase in the proportion of patients with ASA 3 or more.

Patient, tumour and surgery-related aspects in patients with and without early clinical leakage in the 48 centres with 10 or more patients registered in the database are presented in Table 1. None of the chosen risk factors, i.e. sex, age > 60 years, ASA 3 or more and BMI > 25 kg/m², was found to be related to AL in univariate analysis. In contrast, perioperative blood transfusion and absence of neoadjuvant radio(chemo)therapy or defunctioning stoma at primary surgery occurred significantly more frequently in patients with AL. Thus, neoadjuvant radio(chemo)therapy was inversely associated with AL, i.e. neoadjuvant treatment had been administered to a lower percentage of patients with AL than to patients without AL (Table 1).

Early AL grade B and C had a major impact. Reoperation for AL was needed in 86.8% of patients with AL (95% CI 80.7%–92.8%). The mean postoperative length of hospital stay increased from 14.7 days (95% CI 13.1–16.3) in patients without AL to 32.4 days in patients with AL (95% CI 28.7–36.1; $P < 0.001$), and in-hospital mortality rose from 1.1% (95% CI 0.6%–1.6%) to 4.8% (95% CI 1.1%–8.5%; $P < 0.001$).

Although male gender, age > 60 years, ASA 3 or more and BMI > 25 kg/m² were not found to be related to AL in this patient series, variability of AL rates between centres was evaluated before and after adjustment for these factors. No significant variability was observed based on a normal ($P = 0.351$) or non-parametric distribution ($P = 0.246$) for the true centre effects. In the latter distribution, the 25th and 75th percentiles were 4.5% and 7.6%. As could be expected, risk adjustment for the above-mentioned factors did not affect the result (Fig. 1). With the funnel plot of the overall AL rate (6.7%), the risk-adjusted AL rate in two centres was above the 95% upper prediction limit and it was above the 75% upper limit in 12 centres (data not shown). An alternative approach aiming at further improvement in the future was assessed. Risk-adjusted AL rates were funnel-plotted around the percentile 25 performance, i.e. 4.5% AL rate (Fig. 2). This level reflects the median true performance of the centres in the better half. Eight centres performed above the upper 95% prediction limits in this setting.

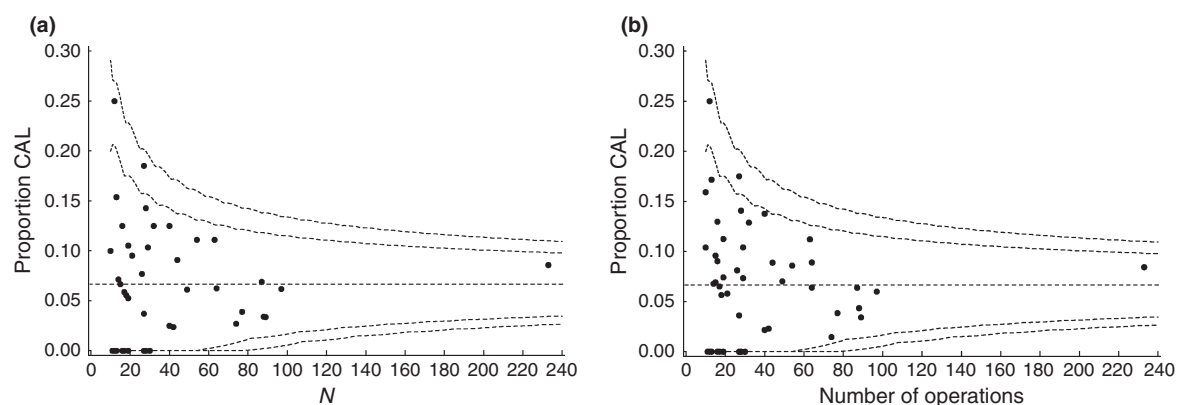
Tumour and surgery-related variables were compared between the better centres (first and second quartile based on prediction limits from the funnel plot around

Table 1 Patient, tumour and surgery-related aspects in patients with and without early clinical leakage in 48 centres with 10 or more patients in the database (percentage if not otherwise indicated).

Data	All patients	Leak*	No leak*	P†
Number of patients	1815	121	1694	
Male	1140 (63)	80 (66)	1060 (63)	0.495
Female	675 (37)	41 (34)	634 (37)	
Mean age (min–max)	65.5 (21–94)	65.5 (32–88)	65.5 (21–94)	0.967
> 60 years	1256/1815 (69)	83 (69)	1173 (69)	0.919
ASA 1 and 2	1052/1366 (77)	87/115 (76)	1279/1565 (82)	0.183
ASA 3 or more	314/1366 (23)	28/115 (24)	286/1565 (18)	
Mean BMI (95% CI)	25.4 (25.2–25.6)	25.8 (24.5–26.9)	25.8 (25.5–26.0)	0.475
BMI < 25	665/1386 (48)	51/100 (51)	614/1286 (48)	0.756
BMI 25 to < 30	519/1386 (37)	34/100 (34)	485/1286 (38)	
BMI 30 or more	202/1386 (15)	15/100 (15)	187/1286 (15)	
Neoadjuvant radio(chemo)therapy	1329/1815 (73)	77/121 (64)	1252/1694 (74)	0.014
ypStage 0	197/1716 (11)	15/115 (13)	182/1601 (11)	0.135
(y)pStage I	460/1716 (27)	24/115 (21)	436/1601 (27)	
(y)pStage II	394/1716 (23)	21/115 (18)	373/1601 (23)	
(y)pStage III	453/1716 (26)	34/115 (30)	419/1601 (26)	
(y)pStage IV	212/1716 (12)	21/115 (18)	191/1601 (12)	
Open reconstruction	1333/1810 (74)	86/121 (71)	1247/1689 (74)	0.506
Laparoscopic or converted reconstruction	477/1810 (26)	35/121 (29)	442/1689 (26)	
Stapled anastomosis	1494/1789 (84)	100/120 (83)	1394/1669 (84)	0.899
Handsewn anastomosis	21/124 (17)	20/120 (17)	275/1669 (16)	
Straight colo-anal anastomosis	628/1815 (35)	43/121 (36)	585/1694 (35)	0.502
Straight CAA with coloplasty	687/1815 (38)	4/121 (3)	58/1694 (3)	
Side-to-end anastomosis	62/1815 (3)	35/121 (29)	403/1694 (24)	
Colon pouch–anal anastomosis	438/1815 (24)	39/121 (32)	648/1694 (38)	
Primary defunctioning stoma	1120/1815 (62)	48/121 (40)	1072/1694 (63)	< 0.001
Perioperative blood transfusion	228/1815 (13)	37/121 (31)	191/1694 (11)	< 0.001

*Because data were not complete for all items, numerators and denominators are presented.

†For the differences between patients with and without anastomotic leakage.

**Figure 1** Funnel plots with observed (a) and risk-adjusted AL rates (b) and 95% and 99% prediction limits around the overall AL rate (6.7%). Each dot represents a centre with 10 or more patients registered.

the overall AL rate) and less well performing centres, i.e. above percentile 50 (Table 2). The better centres more frequently used neoadjuvant treatment, with a positive

effect on tumour stage. They also performed rectal irrigation, completely mobilized the splenic flexure, resected the sigmoid colon more frequently and more

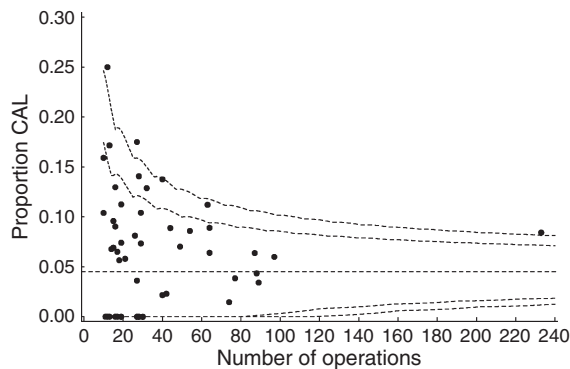


Figure 2 Funnel plot of risk-adjusted AL with 95% and 99% prediction limits around percentile 25 (4.5%) from the non-parametric distribution of the centre levels. Each dot represents a centre with 10 or more patients registered.

frequently routinely constructed a primary defunctioning stoma. In contrast, laparoscopic resection and straight colo-anal anastomoses were performed less frequently, the latter in favour of a colon pouch–anal anastomosis. Their AL rates were low although more patients with low rectal cancer were treated, and hence more handsewn anastomoses were performed.

Discussion

The abdominoperineal excision (APE) rate is a quality of care indicator in rectal cancer surgery. It is certain that sphincter saving *per se* is not the only and maybe not even the most important indicator of the quality of rectal cancer surgery. Moreover, it would be a subjective opinion to decide that a centre with a relatively high

Table 2 Surgery-related aspects in patients treated in risk-adjusted percentile ≤ 50 centres compared with those treated in percentile > 50 centres.

Surgery-related aspects	Percentile ≤ 50 teams*	Percentile > 50 teams*	P
Number of patients	407	886	
Number of rectal cancers in lower rectal third	163/395 (41)	279/869 (32)	0.001
Number of rectal cancers in mid rectal third (5–10 cm)	194/395 (49)	460/869 (53)	
Number of rectal cancers in upper rectal third (> 10 cm)	38/395 (10)	130/869 (15)	
Neoadjuvant treatment for cStage II–III	280/300 (93)	506/612 (83)	< 0.001
ypStage 0	58/400 (15)	78/835 (9)	0.007
(y)pStage I	96/400 (24)	240/835 (29)	
(y)pStage II	106/400 (27)	178/835 (21)	
(y)pStage III	99/400 (25)	241/835 (29)	
(y)pStage IV	41/400 (10)	98/835 (12)	
Rectal irrigation at start or before anastomosis	359/405 (89)	568/883 (64)	< 0.001
<i>En bloc</i> resection of other organs	27/401 (7)	46/886 (5)	0.308
Non <i>en bloc</i> resection of other organs	29/402 (7)	62/885 (7)	0.893
Intra-operative perforation of the rectum (surgeon)	13/401 (3)	26/881 (3)	0.779
Resection of sigmoid colon if no neoadjuvant treatment	277/325 (85)	465/603 (77)	0.003
Resection of sigmoid colon after neoadjuvant treatment	59/77 (77)	201/274 (73)	0.563
Complete mobilization of splenic flexure	362/403 (90)	646/879 (73)	< 0.001
Problems during resection (yes)	51/382 (13)	80/819 (10)	0.064
Open reconstruction	318/407 (78)	625/881 (71)	0.007
Laparoscopic or converted reconstruction	89/407 (22)	256/881 (29)	
Stapled anastomosis	332/400 (83)	776/873 (89)	0.004
Handsewn anastomosis	68/400 (17)	97/873 (11)	
Straight colo-anal anastomosis	103/407 (25)	364/886 (41)	< 0.001
Straight colo-anal anastomosis with coloplasty	19/407 (5)	23/886 (3)	
Side-to-end anastomosis	112/407 (28)	234/886 (26)	
Colon pouch–anal anastomosis	173/407 (43)	265/886 (30)	
Primary defunctioning stoma present	300/407 (74)	586/886 (66)	0.007
Routine stoma (as mentioned)	230/286 (80)	339/568 (60)	< 0.001
Selective stoma (as mentioned)	56/286 (20)	229/568 (40)	
Perioperative blood transfusion (intra-operative or postoperative)	42/407 (10)	109/886 (12)	0.302

Percentile 50 is the percentile of the expected distribution in the funnel plot around the overall AL rate.

*Because data were not complete for all items, numerators and denominators are presented with percentages in parentheses if not otherwise indicated.

AL rate following TME is a poor one if its APE rate is very low. Conversely, a centre with a high APE rate and a low AL rate is not desirable. Thus, several quality of care indicators should be considered when appreciating the quality of performance. This report focused on AL after TME with sphincter-saving reconstruction as observed in centres participating in an improvement project. The impact of AL on postoperative morbidity and mortality is considerable [12,13,17]. In the present survey, AL resulted in an increase of more than 80% in reoperation rates, a prolongation of the length of stay by 17 days and a 3.7% increased mortality. Moreover, AL could delay or prevent the administration of adjuvant chemotherapy and closure of a defunctioning stoma [36]. Thus, reducing the AL rate and its consequences is important for many reasons. Moreover, it is a factor over which surgeons largely have control. It therefore became the basis of a quality improvement strategy and the rationale of the present study.

The overall AL rate of 6.7% in this study was low, but has to be interpreted with caution. Participation in the PROCARE project was not compulsory and registration of patients is not complete. Merging of the PROCARE database with administrative databases indicated that 34% of patients who underwent TME with colo-anal reanastomosis between 2006 and 2008 were not registered in PROCARE. Thus, registration bias cannot be excluded, but also cannot be verified because of the absence of clinical data in administrative databases. Incomplete registration may be related to the fact that not all surgeons in a given centre registered their patients, owing to forgetfulness or lack of time and/or resources to fill in the forms for all patients. Population-based surveys are more complete and reported higher AL rates of 12% [12], 11.6% [13] and 10.9% [17], but all included partial mesorectal excision, known to have a lower AL rate than TME with colo-anal anastomosis. However, in the context of a national improvement project with an educational character, the overall rate is less important than benchmarking participating centres and identification of those aspects that can be improved.

To our knowledge, this is the first study on postoperative AL after TME to report benchmarking of individual centres participating in an improvement initiative. When measuring quality of care indicators, such as AL, risk adjustment for confounding factors is warranted for objective benchmarking. Multivariable analyses of data in large patient series have identified several factors independently related to or associated with AL. Although these factors may explain or predict the occurrence of AL, they are to be selected for benchmarking of the performance in different centres. Indeed, some of the factors are not acceptable for

adjustment at benchmarking from a patient's and a professional point of view and in the context of an improvement project with an educational character. Without knowledge of the results of the analysis, it was decided to adjust only for male gender, age > 60 years, ASA 3 or more and BMI > 25 kg/m². Admittedly, data on pulmonary disease, smoking, diabetes mellitus and coronary heart disease were not available in the database, but they are somehow covered by the patient's ASA classification. Neoadjuvant radio(chemo)therapy was not selected because of its controversial effect on AL. The unexpectedly inverse relation between neoadjuvant therapy and leakage is at least partially explained by the mediating effect of the presence of a defunctioning stoma. Indeed, there was a positive relationship between neoadjuvant therapy and the presence of a defunctioning stoma: 68% of the patients with neoadjuvant therapy had a stoma, compared with 44% of the patients without neoadjuvant therapy ($P < 0.001$).

In the univariable model, the OR for the effect of neoadjuvant therapy on AL was 0.62 (95% CI 0.42–0.91). In a bivariable model with neoadjuvant therapy and presence of stoma as predictors for AL, the strength of this relation became non-significant (OR = 0.76, 95% CI 0.51–1.13, $P = 0.18$), whereas the effect of stoma was significant (OR = 0.40, 95% CI 0.27–0.59, $P < 0.0001$). Besides neoadjuvant treatment and the presence of a primary defunctioning stoma, perioperative blood transfusion also was significantly related to AL in univariate analysis. As mentioned, these factors were not considered for adjustment before analysis because they are aspects of rectal cancer management that depend on tumour stage, surgical skill and decision-making. However, the pre-defined adjustment factors including male gender, age > 60 years, ASA 3 or more and BMI > 25 kg/m² were not found to be related to AL. Consequently no statistically significant variability of AL rates between centres was observed, neither before nor after adjustment for these factors. Wide confidence intervals and overlap with median overall performance were related to low event rate and mainly to the small number of patients in many participating centres. Nonetheless, the absence of statistically significant variability is reassuring, with some reservation due to incomplete registration. Although 'true' variability between centres was statistically not significant, variability exceeding the sampling variability was observed. Statistical non-significance does not imply that the true performance levels of the centres do not differ and that there will be no potential for improvement, at least in some centres.

While statistical confidence is warranted in the context of audit with a repressive, sanctioning character, 99%

limits and league table ranking of performances are less appropriate in projects aiming at quality improvement through educational feedback. In the present report, 95% upper limits around the overall AL rate were preferred, although 99% predicted limits were also shown. No centre performed above the 99% limit. In order to explore opportunities for improvement, tumour and treatment-related aspects were compared between centres performing below and above the adjusted 50th percentile performance of the overall AL rate. It is evident that scoring above the 99% CI of this 'aspirational' benchmark does not reflect poor performance but indicates that there is an opportunity for relevant improvement. Setting the target for improvement at that level should be achievable by many centres with less good performance. Risk-adjusted good performance was not tumour-related but seemed to be related to surgical technical aspects. Centres with a less good performance may have to adopt some technical aspects of the peers with better performances. An internal audit of AL rate and its consequences is most certainly warranted when a selective approach to primary defunctioning stoma construction is applied [37].

Besides incomplete registration of patients by the centres participating in a national project on a voluntary basis, this study has some other limitations and shortcomings. AL rates are reported per centre, although surgery was performed by several surgeons in most (34/48, 71%) of them. In PROCARE, the decision to perform an internal audit was deliberately left to the participating teams. Late ALs diagnosed after hospital discharge were not included in this study. In the Swedish randomized multicentre trial 18 out of 45 ALs were diagnosed after hospital discharge [38,39]. At explorative analysis, late AL was reported in 1.7% of a subset of 750 patients in the present study. This low sampled rate of post-discharge leakage seems contradictory to the Swedish studies but may be related to a longer length of initial hospital stay in Belgium, giving a greater likelihood of a leak being diagnosed prior to discharge. It was decided not to include late ALs for analysis because of their small number and mainly because their morbidity and treatment may be quite different, although not necessarily less important, from those of early leaks.

In conclusion, early AL-related morbidity and mortality are considerable. At this stage of the project, the low early AL rate and the absence of statistically significant risk-adjusted variability between centres are reassuring, but with some reservation related to incomplete registration. Statistical non-significance, however, does not imply that the true performance levels of the centres do not differ and that there is no better 'half of the class'. There is room for improvement. More specifically, some surgical aspects related to colo-anal recon-

struction were found to be associated with the lower incidence of ALs in better performing centres and could be adopted by less well performing centres.

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References

- 1 Martling AL, Holm T, Rutqvist LE, Moran BJ, Heald RJ, Cedemark B. Effect of a surgical training programme on outcome of rectal cancer in the County of Stockholm. Stockholm colorectal cancer study group, Basingstoke bowel cancer research project. *Lancet* 2000; **356**: 93–6.
- 2 Engel AF, Oomen JL, Eijssbouts QA, Cuesta MA, van de Velde CJ. Nationwide decline in annual numbers of abdomino-perineal resections: effect of a successful national trial? *Colorectal Dis* 2003; **5**: 180–4.
- 3 Matthiessen P, Hallböök O, Rutegård J, Sjö Dahl R. Population-based study of risk factors for postoperative death after

- anterior resection of the rectum. *Br J Surg* 2006; **93**: 498–503.
- 4 Khan AA, Wheeler JM, Cunningham C, George B, Kettlewell M, Mortensen NJ. The management and outcome of anastomotic leaks in colorectal surgery. *Colorectal Dis* 2008; **10**: 587–92.
 - 5 Bertelsen CA, Andreassen AH, Jørgensen T, Harling H; Danish Colorectal Cancer Group. Anastomotic leakage after curative anterior resection for rectal cancer: short and long-term outcome. *Colorectal Dis* 2010; **12**: e76–81.
 - 6 Boccola MA, Buettner PG, Rozen WM *et al.* Risk factors and outcomes for anastomotic leakage in colorectal surgery: a single-institution analysis of 1576 patients. *World J Surg* 2011; **35**: 186–95.
 - 7 Gagliardi AR, Simunovic M, Langer B *et al.* Development of quality indicators for colorectal cancer surgery, using a 3-step modified Delphi approach. *Can J Surg* 2005; **48**: 441–52.
 - 8 Malin JL, Schneider EC, Epstein AM, Adams J, Emanuel EJ, Kahn KL. Results of the National Initiative for cancer care quality: how can we improve the quality of cancer care in the United States? *J Clin Oncol* 2006; **24**: 626–34. Erratum in: *J Clin Oncol* 2006; **24**: 1966.
 - 9 Patwardhan MB, Samsa GP, McCrory DC *et al.* Cancer care quality measures: diagnosis and treatment of colorectal cancer. *Evid Rep Technol Assess* 2006; **138**: 1–116.
 - 10 Bittner R, Burghardt J, Gross E *et al.* Qualitätsindikatoren bei Diagnostik und Therapie des Rektumkarzinoms. *Zentralbl Chir* 2007; **132**: 85–94.
 - 11 Vlayen J, Verstreken M, Mertens C, Van Eycken E, Penninckx F (2008) Quality of rectal cancer care. Phase 2: development and testing of a set of quality indicators. *Good Clinical Practice (GCP)*. KCE reports 81A (D/2008/10.273/38), Federaal Kenniscentrum voor de Gezondheidszorg (KCE), Brussel.
 - 12 Matthiessen P, Hallböök O, Andersson M, Rutegård J, Sjødahl R. Risk factors for anastomotic leakage after anterior resection of the rectum. *Colorectal Dis* 2004; **6**: 462–9.
 - 13 Eriksen MT, Wibe A, Norstein J, Haffner J, Wiig JN; Norwegian Rectal Cancer Group. Anastomotic leakage following routine mesorectal excision for rectal cancer in a national cohort of patients. *Colorectal Dis* 2005; **7**: 51–7.
 - 14 Jestin P, Pålman L, Gunnarsson U. Risk factors for anastomotic leakage after rectal cancer surgery: a case-control study. *Colorectal Dis* 2008; **10**: 715–21.
 - 15 Jung SH, Yu CS, Choi PW *et al.* Risk factors and oncologic impact of anastomotic leakage after rectal cancer surgery. *Dis Colon Rectum* 2008; **51**: 902–8.
 - 16 Lee WS, Yun SH, Roh YN *et al.* Risk factors and clinical outcome for anastomotic leakage after total mesorectal excision for rectal cancer. *World J Surg* 2008; **32**: 1124–9.
 - 17 Bertelsen CA, Andreassen AH, Jørgensen T, Harling H; Danish Colorectal Cancer Group. Anastomotic leakage after anterior resection for rectal cancer: risk factors. *Colorectal Dis* 2010; **12**: 37–43.
 - 18 Swedish Rectal Cancer Trial. Initial report from a Swedish multicentre study examining the role of preoperative irradiation in the treatment of patients with resectable rectal carcinoma. *Br J Surg* 1993; **80**: 1333–6.
 - 19 Kapiteijn E, Kranenburg EK, Steup WH *et al.* Total mesorectal excision (TME) with or without preoperative radiotherapy in the treatment of primary rectal cancer. Prospective randomised trial with standard operative and histopathological techniques. Dutch ColoRectal Cancer Group. *Eur J Surg* 1999; **165**: 410–20.
 - 20 Sauer R, Fietkau R, Wittekind C *et al.* Adjuvant versus neoadjuvant radiochemotherapy for locally advanced rectal cancer. A progress report of a phase-III randomized trial (protocol CAO/ARO/AIO-94). *Strahlenther Onkol* 2001; **177**: 173–81.
 - 21 Sebag-Montefiore D, Stephens RJ, Steele R *et al.* Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. *Lancet* 2009; **373**: 811–20.
 - 22 Garlipp B, Ptok H, Schmidt U, Meyer F, Gastinger I, Lippert H. Neoadjuvant chemoradiotherapy for rectal carcinoma: effects on anastomotic leak rate and postoperative bladder dysfunction after non-emergency sphincter-preserving anterior rectal resection. Results of the Quality Assurance in Rectal Cancer Surgery multicenter observational trial. *Langenbecks Arch Surg* 2010; **395**: 1031–8.
 - 23 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**: 355–8.
 - 24 Xiao L, Zhang WB, Jiang PC *et al.* Can transanal tube placement after anterior resection for rectal carcinoma reduce anastomotic leakage rate? A single-institution prospective randomized study. *World J Surg* 2011; **35**: 1367–77.
 - 25 Akasu T, Takawa M, Yamamoto S, Yamaguchi T, Fujita S, Moriya Y. Risk factors for anastomotic leakage following intersphincteric resection for very low rectal adenocarcinoma. *J Gastrointest Surg* 2010; **14**: 104–11.
 - 26 Cong ZJ, Fu CG, Wang HT, Liu LJ, Zhang W, Wang H. Influencing factors of symptomatic anastomotic leakage after anterior resection of the rectum for cancer. *World J Surg* 2009; **33**: 1292–7.
 - 27 Kruschewski M, Rieger H, Pohlen U, Hotz HG, Buhr HJ. Risk factors for clinical anastomotic leakage and postoperative mortality in elective surgery for rectal cancer. *Int J Colorectal Dis* 2007; **22**: 919–27.
 - 28 Eberl T, Jagoditsch M, Klingler A, Tschmelitsch J. Risk factors for anastomotic leakage after resection for rectal cancer. *Am J Surg* 2008; **196**: 592–8.
 - 29 Huh JW, Kim HR, Kim YJ. Anastomotic leakage after laparoscopic resection of rectal cancer: the impact of fibrin glue. *Am J Surg* 2010; **199**: 435–41.
 - 30 Ito M, Sugito M, Kobayashi A, Nishizawa Y, Tsunoda Y, Saito N. Relationship between multiple numbers of stapler firings during rectal division and anastomotic leakage after laparoscopic rectal resection. *Int J Colorectal Dis* 2008; **23**: 703–7.
 - 31 Rahbari NN, Weitz J, Hohenberger W *et al.* Definition and grading of anastomotic leakage following anterior resection

- of the rectum: a proposal by the International Study Group of Rectal Cancer. *Surgery* 2010; **147**: 339–51.
- 32 Spiegelhalter D. Funnel plots for comparing institutional performance. *Stat Med* 2005; **24**: 1185–202.
 - 33 Wong G, Mason W. The hierarchical logistic regression model for multilevel analysis. *JASA* 1985; **80**: 513–24.
 - 34 Thomas N, Longford NT, Rolph JE. Empirical Bayes methods for estimating hospital-specific mortality rates. *Stat Med* 1994; **13**: 889–903.
 - 35 Böhning D (1999) Computer-assisted analysis of mixtures and applications: meta-analysis, disease mapping and others. *Monographs on Statistics and Applied Probability*, p. 81. Chapman & Hall/CRC, Boca Raton, FL.
 - 36 den Dulk M, Smit M, Peeters KC *et al*; Dutch Colorectal Cancer Group. A multivariate analysis of limiting factors for stoma reversal in patients with rectal cancer entered into the total mesorectal excision (TME) trial: a retrospective study. *Lancet Oncol* 2007; **8**: 297–303.
 - 37 Pata G, D'Hoore A, Fieuws S, Penninckx F. Mortality risk analysis following routine *vs* selective defunctioning stoma formation after total mesorectal excision for rectal cancer. *Colorectal Dis* 2009; **11**: 797–805.
 - 38 Matthiessen P, Hallböök O, Rutegård J, Simert G, Sjö Dahl R. Defunctioning stoma reduces symptomatic anastomotic leakage after low anterior resection of the rectum for cancer: a randomized multicenter trial. *Ann Surg* 2007; **246**: 207–14.
 - 39 Matthiessen P, Lindgren R, Hallböök O, Rutegård J, Sjö Dahl R; Rectal Cancer Trial on Defunctioning Stoma Study Group. Symptomatic anastomotic leakage diagnosed after hospital discharge following low anterior resection for rectal cancer. *Colorectal Dis* 2010; **12**: e82–7.