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ORIGINAL CONTRIBUTION

How Should the Low Anterior Resection Syndrome Score Be Interpreted?

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BACKGROUND: Bowel dysfunction after low anterior resection is often assessed by determining the low anterior resection syndrome score. What is unknown, however, is whether this syndrome is already present in the general population and which nonsurgical factors are associated.

OBJECTIVE: The purpose of this study was to determine the prevalence of minor and major low anterior resection syndrome in the general Dutch population and which other factors are associated with this syndrome.

DESIGN: This was a cross-sectional study.

SETTINGS: The study was conducted within the general Dutch population.

PATIENTS: The Groningen Defecation and Fecal Continence Questionnaire was distributed among a general Dutch population-based sample (N = 1259).

MAIN OUTCOME MEASURES: Minor and major low anterior resection syndrome were classified according to the scores obtained.

RESULTS: The median, overall score was 16 (range, 0–42). Minor low anterior resection syndrome was more prevalent than the major form (24.3% vs 12.2%; $p < 0.001$). Bowel disorders, including fecal incontinence, constipation, and irritable bowel syndrome were associated with the syndrome, whereas sex, age, BMI, and vaginal delivery were not. Remarkably, patients with diabetes mellitus were significantly more prone to experience minor or major low anterior resection syndrome. The ORs were 2.8 (95% CI, 1.8–4.4) and 3.7 (95% CI, 2.2–6.2).

LIMITATIONS: We selected frequent comorbidities and other patient-related factors that possibly influence the syndrome. Additional important factors do exist and require future research.

CONCLUSIONS: Minor and major low anterior resection syndrome occur in a large portion of the general Dutch population and even in a healthy subgroup. This implies that the low anterior resection syndrome score can only be used to interpret the functional result of the low anterior resection provided that a baseline measurement of each individual is available. Furthermore, because people with low anterior resection syndrome often experience constipation and/or fecal incontinence, direct examination and diagnosis of these conditions might be a more efficient approach to treating patient bowel dysfunctions. See **Video Abstract** at http://links.lww.com/DCR/B110.

¿CÓMO DEBE INTERPRETARSE LA PUNTUACIÓN DEL SÍNDROME DE RESECCIÓN ANTERIOR BAJA?

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ANTECEDENTES: La disfunción intestinal después de la resección anterior baja a menudo se evalúa determinando la puntuación del síndrome de resección anterior baja. Sin embargo, lo que se desconoce es si este síndrome ya está presente en la población general y qué factores no quirúrgicos están asociados.

OBJETIVO: Determinar la prevalencia del síndrome de resección anterior baja menor y mayor en la población holandesa general y qué otros factores están asociados con este síndrome.

DISEÑO: Estudio transversal.

CONFIGURACIÓN: Población holandesa general.

PACIENTES: El cuestionario de defecación y continencia fecal de Groningen se distribuyó entre una muestra general de población holandesa (N = 1259).

PRINCIPALES MEDIDAS DE RESULTADO: El síndrome de resección anterior baja menor y mayor se clasificó de acuerdo con las puntuaciones obtenidas.

RESULTADOS: La mediana de la puntuación general fue de 16.0 (rango 0-42). El síndrome de resección anterior baja menor fue más frecuente que la forma principal (24.3% versus 12.2%, (P <0.001). Los trastornos intestinales, incluyendo incontinencia fecal, estreñimiento y síndrome del intestino irritable se asociaron con el síndrome, mientras que el sexo, la edad y el cuerpo el índice de masa y el parto vaginal no lo hicieron. Notablemente, los pacientes con diabetes mellitus fueron significativamente más propensos a experimentar el síndrome de resección anterior baja menor o mayor. Las razones de probabilidad fueron 2.8 (IC 95%, 1.8-4.4) y 3.7 (IC 95%, 2.2 -6.2), respectivamente.

LIMITACIONES: Se seleccionaron las comorbilidades frecuentes y otros factores relacionados con el paciente que posiblemente influyen en el síndrome. Existen otros factores importantes que requieren investigación en el futuro.

CONCLUSIONES: El síndrome de resección anterior baja menor y mayor ocurre en una gran parte de la población holandesa general e incluso en un subgrupo sano. Esto implica que la puntuación del síndrome de resección anterior baja solo se puede utilizar para interpretar el resultado funcional de la resección anterior baja, siempre que esté disponible una medición inicial de cada individuo. Además, dado que las personas con síndrome de resección anterior baja a menudo experimentan estreñimiento y/o incontinencia fecal, el examen directo y el diagnóstico de estas afecciones pueden ser un enfoque más eficiente para tratar las disfunciones intestinales de los pacientes. Consulte **Video Resumen** en http://links.lww.com/DCR/B110. (*Traducción—Dr. Gonzalo Hagerman*)

KEY WORDS: Anterior resection; Bowel dysfunction; Low anterior resection syndrome; Rectal cancer.

Low anterior resection is a common colorectal surgical procedure. Nevertheless, many patients report severe postoperative bowel dysfunction. It is assumed that the bowel complaints arise subsequent to the resection.[1,2] As a consequence, this complex of bowel complaints is referred to as low anterior resection syndrome (LARS). It is manifested by a broad spectrum of symptoms, including incontinence for flatus and/or liquid stool, clustering of stools, fecal urgency, and an extremely high or low frequency of bowel movements.[1]

The LARS score was designed in 2012 as a quick tool to assess functional outcome of patients after low anterior resection for rectal cancer.[3] Subsequently, the LARS score was translated into different languages and validated for different countries and has become a frequently used tool in both clinical practice and research.[4–6] The prevalence of minor LARS after low anterior resection for rectal cancer is between 22% and 28%. The prevalence for major LARS is between 38% and 62%.[6] Remarkably, a recent article by Juul et al[7] stated that major LARS is not restricted to patients who had undergone a low anterior resection. It also occurs in the general population, where prevalence is highest, up to 18.8%, in 50- to 79-year–old women.[7] As far as we know, the prevalence of minor LARS in the general population has not yet been described.

Bowel dysfunction is not only caused by abdominal surgery; age and sex are 2 other known influences.[8] It is unclear what extent these factors and others, such as obstetric history or comorbidities, contribute to LARS symptoms. It would seem that the current use and interpretation of the LARS score requires refinement.

Our first aim therefore was to explore the prevalence of minor and major LARS in the general Dutch population and in a subpopulation without the comorbidities known to influence bowel function. Second, we aimed to determine which factors, other than low anterior resection, contribute significantly to minor or major LARS.

PATIENTS AND METHODS

Study Design

For this retrospective cross-sectional study, Survey Sampling International (Rotterdam, the Netherlands) invited members of the general Dutch population to fill out the digital Defecation and Fecal Continence Questionnaire in 2015 to form a population-based sample (N = 1259).[9,10] A random selection of the respondents was made to arrive at a representative cohort according to the population pyramid of the Netherlands, with sex, age, and region equally distributed.[9] The survey was designed in such a way that all of the questions had to be answered, thus yielding

a database without missing data. The completed questionnaires provided us with a comprehensive overview of bowel functioning and possible bowel-related symptoms, including LARS symptoms. The Defecation and Fecal Continence Questionnaire has been validated in the Dutch population.[10]

Study Groups

First, we analyzed the entire sample irrespective of respondents' medical history. Second, we performed a subanalysis of 2 subgroups formed on the basis of comorbidities known to influence bowel function. This subanalysis was performed to estimate the prevalence of LARS in respondents whose bowel functions were, at least theoretically, healthy. Therefore, the subgroup without comorbidities consisted of the respondents who had reported not having any comorbidities known to influence bowel function, such as surgery for bowel (n = 32), fistula (n = 15), anus (n = 16), hemorrhoids (n = 28), prostate (n = 16), Hirschsprung disease (n = 3), teratomas (n = 1), or vaginal and abdominal hysterectomy (n = 75). Respondents who reported experiencing one of the following comorbidities, which are known to influence bowel function, were also excluded from this subgroup: Crohn's disease or ulcerative colitis (n = 14), irritable bowel syndrome (IBS; n = 99), rectal prolapse (n = 17), diabetes mellitus (n = 114), cerebrovascular accidents (n = 20), neurologic disorders (n = 18), slow transit constipation (n = 6), anorectal malformation (n = 1), sacrococcygeal teratoma (n = 2), or spina bifida (n = 1). The comorbidities subgroup consisted of the respondents who had reported experiencing at least 1 of the above-mentioned comorbidities.

Assessment of Fecal Disorders

We diagnosed minor and major LARS based on 5 items of the LARS score, as described by Emmertsen and Laurberg[3]: incontinence for flatus and/or liquid stool, frequency of bowel movements, clustering of the stools, and fecal urgency. Respondents who scored <21 points did not have LARS. Respondents who scored 21 to 29 points experienced minor LARS, whereas 30 to 42 points indicated major LARS.

We defined constipation, fecal incontinence (FI), and IBS in accordance with the Rome IV criteria.[11,12] In case of constipation, respondents had to comply with at least 2 of these criteria during the last 3 months, with symptom onset at least 6 months before diagnosis: >25% defecation straining, lumpy or hard stools, incomplete evacuation, anorectal blockage, manual maneuvers to support defecation, <3 spontaneous bowel movements per week, and loose stools rarely present without previous use of laxatives. To meet the criteria for FI, respondents had to experience recurrent involuntary passage of fecal material (solid or liquid stool), including soiling, occurring at least 2 to 4 times during 4 weeks over the last 6 months. In case of IBS, respondents had to comply with at least 2 of the following criteria: recurrent abdominal pain on average at least 1 day per week during the last 3 months and associated with 2 or more of the following: defecation, a change in stool frequency, and a change in the appearance of stool.

Statistical Analysis

IBM SPSS Statistics, version 23.0 (IBM Corp, Armonk, NY), was used for statistical analyses. The data represented by continuous variables were not distributed normally and are presented as medians with ranges. The Kruskall–Wallis test was used to compare such data. Categorical variables were presented as numbers and percentages. Comparisons were made using the χ^2 test in case of categorical variables. Univariate and multivariate regression analyses were used to determine the ORs with the corresponding 95% CIs, where justified. The level of statistical significance was set at $p < 0.05$.

Ethical Approval

The study was conducted in compliance with the requirements of the medical ethical review board of the University Medical Center Groningen, the Netherlands.

RESULTS

Respondent Characteristics, the Prevalence of LARS, and Potential Influencing Factors

The total study population (N = 1259) consisted of 579 men (46%) and 680 women (54%) with a median age of 49 years (range, 18–85 y). All of the respondent characteristics are shown in Table 1.

LARS in the General Dutch Population

We found that the sample representing the general Dutch population had a median LARS score of 16, ranging between 0 and 42. As Table 1 shows, 36.5% of the respondents experienced LARS, with minor LARS significantly more prevalent than major LARS (24.3% vs 12.2%; $p < 0.001$). Minor and major LARS were slightly more prevalent among women than men. Sex, age, and BMI were not significantly associated with LARS ($p = 0.155$, $p = 0.111$, and $p = 0.415$).

Bowel Dysfunctions Associated With LARS

Constipation and FI were significantly associated with minor LARS ($p < 0.005$ and $p < 0.001$), whereas the association with IBS was not significant. Univariate regression analysis confirmed that respondents with constipation or FI were 1.65 and 6.33 times more prone to experience minor LARS than respondents who did not have such dysfunctions (Table 2). As expected, the prevalence of constipation, FI, and IBS was highest in the respondents experiencing major LARS (43.1%, 35.9%, and 13.7%; Table 1). Univariate analysis confirmed that respondents

TABLE 1. The prevalence of LARS and of the potentially associated factors

Factors	*Total*	*No LARS*	*Minor LARS*	*Major LARS*
LARS prevalence, n (%)	1259 (100)	800 (63.5)	306 (24.3)	153 (12.2)
Demographic factors				
Sex, n (%)				
Men	579 (46.0)	384 (66.3)	132 (22.8)	63 (10.9)
Women	680 (54.0)	416 (61.2)	174 (25.6)	90 (13.2)
Age, median (range), y	49 (18–85)	50 (18–85)	50 (18–85)	46 (18–78)
BMI, median (range), kg/m^2	25.5 (13.4–65.3)	25.5 (15.0–45.8)	25.6 (13.4–60.2)	25.6 (16.3–65.3)
Associated bowel dysfunctions, n (%)				
Constipation	235 (18.7)	107 (13.4)	62 (20.3)	66 (43.1)
Fecal incontinence	100 (7.9)	14 (1.8)	31 (10.1)	55 (35.9)
Irritable bowel syndrome	57 (4.5)	23 (2.9)	13 (4.2)	21 (13.7)
Medication that could influence bowel function, n (%)				
Laxatives*	85 (6.8)	27 (3.4)	22 (7.2)	36 (23.5)
Antidiarrheal drugs*	23 (1.8)	1 (0.1)	6 (2.0)	16 (10.5)
Obstetric history				
Vaginal birth, n (%)				
0	896 (71.2)	574 (71.8)	217 (70.9)	105 (68.6)
≥1	363 (28.8)	226 (28.3)	89 (29.1)	48 (31.4)
Comorbidities, n (%)				
Diabetes mellitus	114 (9.1)	44 (5.5)	43 (14.1)	27 (17.6)
Cerebrovascular accident	20(1.6)	13(1.6)	5 (1.6)	2 (1.3)

LARS = low anterior resection syndrome. Prevalences are reported as medians.
*Medications were used at least several times per month.

who had these bowel dysfunctions were more likely to experience major LARS than respondents without these dysfunctions (Table 2). Consequently, the use of laxatives and antidiarrheal medication was also highest in the group with major LARS (Table 1). The respondents who used laxatives or antidiarrheal medication were ≈9 to 93 times more prone to experience major LARS than respondents who did not use such medication (Table 2).

Other Factors Potentially Associated With LARS

Remarkably, when considering diabetes mellitus, we found that it was associated with both types of LARS

TABLE 2. Univariate analysis of potential factors influencing LARS

	Minor LARS		*Major LARS*	
Factors	*OR (95% CI)*	*p*	*OR (95% CI)*	*p*
Associated bowel dysfunction				
Constipation		<0.005		<0.001
No	Reference		Reference	
Yes	1.65 (1.17–2.32)		4.91 (3.36–7.18)	
Fecal incontinence		<0.001		<0.001
No	Reference		Reference	
Yes	6.33 (3.32–12.07)		31.51 (16.9–58.76)	
Irritable bowel syndrome		0.25		<0.001
No	Reference		Reference	
Yes	1.5 (0.75–3.00)		5.38 (2.89–9.99)	
Medication used in case of bowel dysfunctions				
Laxatives*		0.007		<0.001
No	Reference		Reference	
Yes	2.22 (1.24–3.96)		8.81 (5.16–15.05)	
Antidiarrheal drugs*		0.01		<0.001
No	Reference		Reference	
Yes	15.98 (1.92–133.29)		93.31 (12.28–709.36)	
Comorbidities				
Diabetes mellitus		<0.001		<0.001
No	Reference		Reference	
Yes	2.81 (1.80–4.38)		3.68 (2.2–6.16)	

LARS = low anterior resection syndrome.
*Medications were used at least several times per month.

TABLE 3. The prevalence of LARS in the subgroups with and without comorbidities

LARS status	*Total study group, n (%)*	*Subgroup without comorbidities, n (%)*	*Subgroup with comorbidities, n (%)*
Total	1259 (100)	884 (100)	375 (100)
No LARS	800 (63.5)	613 (69.3)	187 (49.9)
Minor LARS	306 (24.3)	192 (21.7)	114 (30.4)
Major LARS	153 (12.2)	79 (8.9)	74 (19.7)

LARS = low anterior resection syndrome. Prevalences are reported as medians.

($p < 0.001$). The prevalence of minor and major LARS among respondents with diabetes mellitus was 37.7% and 23.7%. Respondents who had diabetes mellitus were ≈3 times more prone to experience minor LARS in comparison with the respondents without diabetes mellitus (Table 2). Moreover, these respondents were 3.7 times more likely to experience major LARS than the respondents without diabetes mellitus (Table 2). In contrast, neither cerebrovascular accidents nor vaginal birth were associated with either minor or major LARS.

Prevalence of LARS and Other Bowel Dysfunctions in Relation to Comorbidities

Of the total study population, 884 respondents (70.2%) did not report any comorbidity that could potentially have contributed to the bowel dysfunction specified in the methods. The other 375 respondents (29.8%) had at least 1 of these comorbidities (Table 3). The presence of the comorbidities increased the likelihood of experiencing minor LARS ≈2 times (OR = 1.95 (95% CI, 1.47–2.59); $p < 0.001$) and major LARS 3 times (OR = 3.07 (95% CI, 2.15–4.39); $p < 0.001$). Nevertheless, 21.7% of the respondents without comorbidities experienced minor LARS and 8.9% experienced major LARS. Furthermore, we found that, irrespective of the comorbidities, symptoms typical for constipation were reported most often in cases of minor and major LARS (Fig. 1). Finally, we found the highest prevalence of FI in respondents with major LARS and comorbidities.

DISCUSSION

This study shows that LARS is not restricted to patients who had undergone low anterior resection but that it was also frequent among the general Dutch population. Minor and major LARS even occurred among respondents without any comorbidity that is known to influence bowel function. Furthermore, respondents with diabetes mellitus were significantly more prone to experience minor and major LARS. Therefore, without a baseline and knowledge of the medical background of an individual, minor or major LARS measured after resection should not be interpreted straight away as poor functional outcome after surgery.

It is remarkable to observe that one third of the general Dutch population experiences minor or major LARS, following the LARS score. This prevalence is high, especially when taking into account the prevalences of minor and major LARS after low anterior resection (22%–28% and 38%–62%).[6] The prevalence of LARS in this study was comparable to the recent findings of Juul et al[7] for major LARS among the general Danish population. In our study we also described minor LARS and the relation of LARS with different comorbidities, other types of bowel dysfunction, and medication.

At first, it might be surprising that respondents who had not undergone a low anterior resection experienced LARS. However, when we take into account the relatively high prevalences of different bowel dysfunctions in nonpatient populations, our finding seems to be justified. For example, a Dutch study revealed that 24.5% of the general Dutch population had constipation and 7.9% had FI.[9] Because symptoms included in the LARS score overlap with some symptoms of constipation and FI, the high prevalence of LARS that we found among the general population is not surprising.

Originally, the LARS score was developed as a quick tool to assess the bowel function of patients after resection for rectal cancer.[3] The high frequencies of LARS among the general population clearly show that minor and major LARS were already present in a considerable part of the population before resection. This finding indicates that if the LARS score is considered without determining a baseline, it might be misinterpreted. This in turn raises the question of how to interpret the LARS score to draw an objective conclusion regarding a patient's functional outcome.

One might presume that the LARS score obtained after resection would be more objective if a baseline had been established before surgery. This seems logical, but, as reported by Thomas et al,[13] preoperative screening for LARS is currently performed by perhaps only 10% of the surgeons in the Netherlands. Such unsystematic preoperative screening might stem from the fact that the bowel function of many patients before low anterior resection was affected by rectal cancer, and a LARS score at that moment would not be a true reflection of their baseline.

This brings us to the question of whether normative values obtained from a general population might not be a better option for the baseline, as was proposed by Juul et al.[7] If so, the baseline would require correction for those factors that are significantly associated with LARS. We determined which factors, other than a low anterior resection, significantly contributed to minor or major LARS in the general Dutch population. Previously, age, sex, BMI, and obstetric history were described as being related to LARS.[3,7,14,15] In contrast, we found no significant association between minor or major LARS and these factors. This indicates that

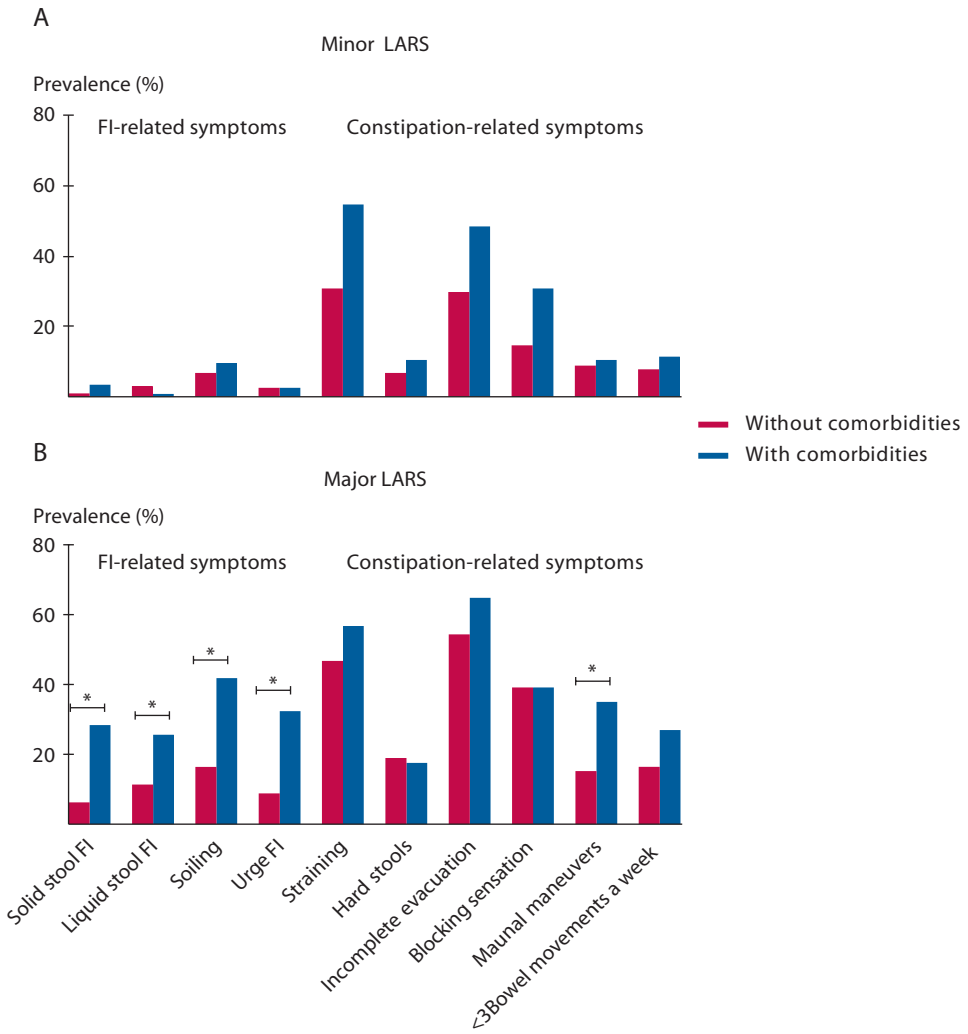

FIGURE 1. The distribution of separate symptoms characteristic of bowel dysfunctions, such as fecal incontinence (FI) and constipation, in respondents experiencing (A) minor LARS and (B) major LARS. LARS = low anterior resection syndrome. Prevalences are reported as medians.

these factors were probably not crucial for establishing the baseline LARS score. The difference of our outcomes, in terms of age and sex as cofactors, might be explained by the fact that we did not investigate patients but rather a sample representing the general population, and the age distribution of such a population is different from that of patients. Furthermore, to investigate whether comorbidities were associated with LARS, we looked at diabetes mellitus and cerebrovascular accidents that are known to occur frequently in the general population. Cerebrovascular accidents were not associated with LARS. Respondents with diabetes mellitus were significantly more prone to experience LARS. Consequently, this comorbidity should be taken into account when interpreting the LARS score.

Knowing that the general Dutch population is not free of comorbidities that can negatively influence bowel function, we also performed the analysis in a subpopulation without comorbidities to estimate the prevalence of LARS in theoretically healthy respondents. Remarkably, the prevalences of minor and major LARS were only slightly lower in this group. Nevertheless, approximately one third of the subpopulation experienced LARS. These observations bring us back to the question: how should we interpret the LARS score after low anterior resection if we know that respondents who never have undergone abdominal operations or experience comorbidities that possibly influence bowel function already experience LARS? Considering the outcomes of this study, we agree with Ribas et al,[16] who already indicated that the LARS score might overestimate the impact of LARS.

Finally, it is important to remember that LARS is a complex, multifactorial syndrome, involving more than FI and impaired bowel frequency.[17,18] It has been shown that even specialists and colorectal care nurses, who routinely deal with patients after low anterior resection, do not have a thorough understanding of their patients' problems in terms of bowel dysfunction.[19] This hampers proper diagnosis and effective treatment. The fact that ≈28% of

the respondents with LARS were also diagnosed with constipation, that ≈19% had FI, and that >7% experienced IBS shows that the LARS score does not provide precise insight into the nature of the bowel problem. Therefore, although the LARS score certainly helps to quickly assess postoperative outcomes, we ask ourselves whether more specific diagnostic investigation, focused directly on constipation and/or FI, would not be more efficient to guide the clinician toward effective treatment of patient bowel dysfunctions.

In this study, we were unable to analyze all of the possible comorbidities and other factors that might influence LARS. We are aware that there are more important factors that warrant future study. Another limitation to this study is that it was restricted to the Dutch population. Nevertheless, our results are in line with recent findings published by Juul et al,[7] who reported on a study conducted in the population of Denmark. We are therefore confident that the main conclusions of this study might be generalized to other countries.

CONCLUSION

Minor and major LARS occur in a large part of the general Dutch population and even in a healthy subgroup. This questions the original purpose for which the LARS score was developed. In our option, the LARS score can only be used to interpret the functional result of low anterior resection when a proper baseline measurement of each individual patient is considered. Moreover, because patients with LARS often experience constipation and/or FI, we ask ourselves whether direct investigation and diagnosis of these 2 conditions might not be more efficient to guide the clinician toward effective treatment of their patients' bowel dysfunctions.

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