

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	“The French LARS score”: Validation of the French version of the low anterior resection syndrome (LARS) score for measuring bowel dysfunction after sphincter-preserving surgery among rectal cancer patients: a study protocol
AUTHORS	Eid, Yassine; Bouvier, Véronique; Dejardin, Olivier; Menahem, Benjamin; Chaillot, Fabien; Chene, Yannick; Dutheil, Jean Jacques; Juul, Therese; Morello, Rémy; Alves, Arnaud

VERSION 1 – REVIEW

REVIEWER	Sigmar Stelzner, M.D., PhD Dresden-Friedrichstadt General Hospital Department of General, Visceral and Thoracic Surgery Friedrichstr. 41 01067 Dresden Germany
REVIEW RETURNED	06-Oct-2019

GENERAL COMMENTS	<p>This study protocol describes the translation and validation of the LARS score in French. For this purpose a comprehensive study of appr. 1000 patients is planned. This study is important because it provides French clinicians and researchers with a very important tool of patient reported outcome measures. The LARS score, initially developed in Denmark, is now available in many languages including English (Juul/Battersby et al. Colorectal Dis 2015), Spanish (Juul/Ahlberg et al. Ann Surg 2014), Chinese (Hou et al. Eur J Oncol Nurs 2015), and German (Bittorf & Matzel, Coloproctology 2015). Since its introduction, it has been widely used for evaluation of functional problems after rectal resection. For international comparison, the French contribution to this topic is indispensable. Therefore, the endeavor to validate a French version is absolutely necessary.</p> <p>The protocol is sound and the psychometric and statistical methods are appropriate.</p> <p>Some minor issues need to be addressed before the manuscript is acceptable for publication:</p> <p>The anticipated number of patients to be enrolled is not clear from the manuscript. In the abstract, n=400 patients are mentioned. In the M&M section, all patients treated from 2007 to 2017 in 34 units are eligible. 400 patients are set for the reliability tests. Lower down, 3000 patients are to be contacted. This should be clarified, especially in the abstract.</p> <p>„bowel fractionation“ should read „bowel movement fractionation“, also referred to as „clustering“</p> <p>“perineural enhancement” suggested reading: “perineural invasion”</p>
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	<p>Please check spelling/grammar: These patients with have primary education levels</p> <p>For discriminant validity testing the extent of procedure (PME vs. TME) should be considered. Along with this, a stratification of neoadjuvant therapy should be done for PME/TME (patients with tumors > 12 cm from the anal verge do usually not undergo neoadjuvant therapy but are treated with PME, which usually results in lower proportions of LARS/majorLARS (see Kupsch et al. Int J Color Dis 2018)).</p> <p>Please check grammar: A search for the ceiling or floor effects will be systematically be made.</p>
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REVIEWER	Lisette Wiltink Leiden University Medical Centre, the Netherlands
REVIEW RETURNED	09-Oct-2019

GENERAL COMMENTS	<p>This protocol is about the validation of the French version of the LARS score. A very relevant topic. Further, the protocol is methodologically sound.</p> <p>A few typo's: page 3, line 1 page 4, line 56 page 14, line 26</p>
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REVIEWER	Ann Van Hecke Ghent University
REVIEW RETURNED	13-Nov-2019

GENERAL COMMENTS	<p>Dear Editor,</p> <p>The authors of the manuscript will validate the French version of the low anterior resection syndrome (LARS) score for measuring bowel dysfunction after sphincter-preserving surgery among rectal cancer patients. The validation and reliability procedures described seemed appropriate and rigorous. However, as editor / journal I would rather prefer the articles with the results of the validation and not only the protocol. I do not know if this is of enough interest for the readers of the journal. Although this might add to our knowledge, I would like to discuss some concerns to consider.</p> <p>1) General impression: a. The manuscript is difficult to read due to some grammatical errors and complex sentence structures. In general, it would benefit them to have the manuscript reviewed by a native or very fluent English speaker for grammar and composition.</p> <p>2) Introduction: a. The authors report that a steady state is reached after about one or two years. Recent studies indicate that some patients suffer from major LARS even after several years. (Chen, T. Y. T., Wiltink, L. M., Nout, R. A., Kranenbarg, E. M. K., Laurberg, S., Marijnen, C. A., & van de Velde, C. J. (2015). Bowel function 14 years after preoperative short-course radiotherapy and total mesorectal excision for rectal cancer: report of a multicenter randomized trial. Clinical colorectal cancer, 14(2), 106-114.)</p> <p>3) Methods: (1) In the inclusion criteria the age is limited to 80 Years old. What is the rationale for this age limitation?</p>
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	(2) Patients will be approached after a minimum duration of 24 months after surgery. Is this regarding the rectal cancer surgery or the reversal of the temporary stoma?
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1:

This study protocol describes the translation and validation of the LARS score in French. For this purpose a comprehensive study of appr. 1000 patients is planned. This study is important because it provides French clinicians and researchers with a very important tool of patient reported outcome measures. The LARS score, initially developed in Denmark, is now available in many languages including English (Juul/Battersby et al. Colorectal Dis 2015), Spanish (Juul/Ahlberg et al. Ann Surg 2014), Chinese (Hou et al. Eur J Oncol Nurs 2015), and German (Bittorf & Matzel, Coloproctology 2015). Since its introduction, it has been widely used for evaluation of functional problems after rectal resection. For international comparison, the French contribution to this topic is indispensable. Therefore, the endeavor to validate a French version is absolutely necessary.

The protocol is sound and the psychometric and statistical methods are appropriate.

1-Some minor issues need to be addressed before the manuscript is acceptable for publication:

The anticipated number of patients to be enrolled is not clear from the manuscript. In the abstract, n=400 patients are mentioned. In the M&M section, all patients treated from 2007 to 2017 in 34 units are eligible. 400 patients are set for the reliability tests. Lower down, 3000 patients are to be contacted. This should be clarified, especially in the abstract.

Response: as suggested by the reviewer, the anticipated number of patients has been clarified in the abstract revised version of the manuscript. « 1000 patients will be enrolled for all the analyses. The questionnaire will be initially administered to the first 100 patients in order to verify the adequacy and degree of comprehension of the questions. Then reproducibility will be investigated by a test-retest procedure in the following 400 patients.

2-„bowel fractionation“ should read „bowel movement fractionation“, also referred to as „clustering“

“perineural enhancement” suggested reading: “perineural invasion”

Response ; the requested editing has been done.

3- Please check spelling/grammar: These patients with have primary education levels

Response: as suggested by the reviewer, the grammar has been checked. "These patients will have primary education levels, secondary education levels, and college or higher education levels and tumour stages I, II and III."

4-For discriminant validity testing the extent of procedure (PME vs. TME) should be considered. Along with this, a stratification of neoadjuvant therapy should be done for PME/TME (patients with tumors > 12 cm from the anal verge do usually not undergo neoadjuvant therapy but are treated with PME, which usually results in lower proportions of LARS/majorLARS (see Kupsch et al. Int J Color Dis 2018)).

Response: as suggested by the reviewer, the extent of the surgical procedure (partial or mesorectal excision) was considered for discriminant validity testing. We agree with the reviewer that stratification of neoadjuvant therapy should be done for partial or total mesorectal excision. These amendments have been added in the revised version of the manuscript.

We have also added the following sentence: "Moreover, interactions with neoadjuvant radiation therapy will be systematically tested. "

5-Please check grammar: A search for the ceiling or floor effects will be systematically be made.

Response: as suggested by the reviewer, the grammar has been checked for this sentence.

Reviewer #2:

1-This protocol is about the validation of the French version of the LARS score. A very relevant topic. Further, the protocol is methodologically sound.

A few typo's:

page 3, line 1

page 4, line 56

page 14, line 26

Response: As suggested by the reviewer, typing errors are now fixed in the manuscript.

Reviewer #3:

Dear Editor,

The authors of the manuscript will validate the French version of the low anterior resection syndrome (LARS) score for measuring bowel dysfunction after sphincter-preserving surgery among rectal cancer patients. The validation and reliability procedures described seemed appropriate and rigorous. However, as editor / journal I would rather prefer the articles with the results of the validation and not only the protocol. I do not know if this is of enough interest for the readers of the journal. Although this might add to our knowledge, I would like to discuss some concerns to consider.

1) General impression:

a. The manuscript is difficult to read due to some grammatical errors and complex sentence structures. In general, it would benefit them to have the manuscript reviewed by a native or very fluent English speaker for grammar and composition.

Response: As suggested by the reviewer, the final version of the manuscript has been totally checked by a native English-speaking copyeditor.

2) Introduction:

a. The authors report that a steady state is reached after about one or two years. Recent studies indicate that some patients suffer from major LARS even after several years. (Chen, T. Y. T., Wiltink, L. M., Nout, R. A., Kranenbarg, E. M. K., Laurberg, S., Marijnen, C. A., & van de Velde, C. J. (2015). Bowel function 14 years after preoperative short-course radiotherapy and total mesorectal excision for rectal cancer: report of a multicenter randomized trial. *Clinical colorectal cancer*, 14(2), 106-114.)

Response: We totally agree with this comment. Three recent studies reported that nearly 40% of patients still experience major LARS symptoms at long-term follow-up.

In the introduction of this paper, we already wrote: "These symptoms usually appear immediately after surgery, become most pronounced during the first few months, improve somewhat thereafter, and reach a steady state after approximately one to two years [11, 12]". Nonetheless, we can add another sentence if necessary.

3) Methods:

(1) In the inclusion criteria the age is limited to 80 Years old. What is the rationale for this age limitation?

As suggested by the reviewers, age > 80 years old) is an exclusion criterion in our study for many reasons.

First, octogenarians suffer from significant comorbidities that exclude them from the majority clinical trials.

Second, they experience worse physical functioning compared to younger patients, as suggested by the study published by Couwenberg and al.*

Third, very few data are available about bowel function in octogenarians following rectal resection with nerve-sparing.

**The impact of postoperative complications on health-related quality of life in older patients with rectal cancer, a prospective cohort study. Couwenberg. Journal of geriatric oncology 9 (2018) 102-109*

(2) Patients will be approached after a minimum duration of 24 months after surgery. Is this regarding the rectal cancer surgery or the reversal of the temporary stoma?

Response: as suggested by the reviewer, bowel continuity (including the reversal of the temporary stoma) restored for at least 24 months is part of the patient inclusion criteria. This sentence has been added in the revised version of the manuscript.

VERSION 2 – REVIEW

REVIEWER	Sigmar Stelzner, M.D. Dresden-Friedrichstadt General Hospital, Germany
REVIEW RETURNED	23-Dec-2019

GENERAL COMMENTS	<p>This study protocol describes the translation and validation of the LARS score in French. For this purpose a comprehensive study of appr. 1000 patients is planned. This study is important because it provides French clinicians and researchers with a very important tool of patient reported outcome measures. The LARS score, initially developed in Denmark, is now available in many languages including English (Juul/Battersby et al. Colorectal Dis 2015), Spanish (Juul/Ahlberg et al. Ann Surg 2014), Chinese (Hou et al. Eur J Oncol Nurs 2015), and German (Bittorf & Matzel, Coloproctology 2015). Since its introduction, it has been widely used for evaluation of functional problems after rectal resection. For international comparison, the French contribution to this topic is indispensable. Therefore, the endeavor to validate a French version is absolutely necessary.</p> <p>The protocol is sound and the psychometric and statistical methods are appropriate.</p> <p>The authors have adaequately responded to the issues raised.</p>
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