Journal of Visceral Surgery (2017) 154, 231—237

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

ORIGINAL ARTICLE

Impact of a procalcitonin-based algorithm on the management of adhesion-related small bowel obstruction☆

C. Cossé[a,b,c], C. Sabbagh[a,b], V. Carroni[a], A. Galmiche[d], L. Rebibo[a], J.-M. Regimbeau[a,c,e,*]

[a] *Department of Digestive and Oncological Surgery, Amiens University Medical Center, Jules Verne University of Picardie, Amiens, France*
[b] *INSERM U1088, Jules Verne University of Picardie, Amiens, France*
[c] *Clinical Research Centre, Amiens University Medical Center and Jules Verne University of Picardie, Amiens, France*
[d] *Department of Biochemistry, Amiens University Medical Center and Jules Verne University of Picardie, Amiens, France*
[e] *EA4294, Jules Verne University of Picardie, Amiens, France*

Available online 30 January 2017

KEYWORDS
Procalcitonin;
Adhesion-related small bowel obstruction

Summary
Introduction: Adhesion-related small bowel obstruction (ASBO) management is difficult if there are no signs of strangulation or peritonitis when intestinal transit has not been restored. The aim of the present study was to determine the impact of combining a procalcitonin (PCT)-based algorithm with clinical signs on the management of uncomplicated ASBO.
Method: We performed a pilot, retrospective, single-center ''before—after'' study. During the ''before'' period (2007 to 2012), patients with uncomplicated ASBO ($n = 93$, the Gastrografin® group) underwent a clinical examination and a Gastrografin® index. During the ''after'' period (2013 to 2016), patients with uncomplicated ASBO ($n = 70$, the algorithm group) underwent a clinical examination and were assessed with the PCT-based algorithm. The study's primary outcome was the appropriateness of ASBO management. The secondary outcomes were the need for surgery and the time to surgery, the LOS, the morbidity and mortality rates, and the recurrence rate.
Results: The proportion of well-managed patients was higher in the algorithm group than in the Gastrografin® group (86% vs. 47%; $P < 0.001$). The time to surgery (48 h vs 72 h; $P = 0.02$) and the LOS (4 vs. 6 days, $P = 0.02$) were significantly lower in the algorithm group. The need for surgery was similar in both groups (31% vs. 37%, $P = 0.49$). The morbidity ($P = 0.69$), mortality ($P = 0.82$) and recurrence rates ($P = 0.57$) were similar in the two groups.

Abbreviations: PCT, procalcitonin; ASBO, adhesion-related small bowel obstruction.

☆ This work was presented as an oral communication at the congress of the Indian Association of Surgical Gastroenterology (Pune, October 2015).

* Corresponding author. Department of Digestive and Oncological Surgery. CHU Sud, avenue René-Laennec, 80054 Amiens cedex 01, France. Tel.: +33 322 088905; fax: +33 322 089733.
E-mail address: regimbeau.jean-marc@chu-amiens.fr (J.-M. Regimbeau).

http://dx.doi.org/10.1016/j.jviscsurg.2017.01.004

Conclusion: The use of a PCT-based algorithm is of value in the routine clinical management of ASBO; it reduces the LOS and the time to surgery without increasing the need for surgery.

Introduction

Although acute adhesion-related small bowel obstruction (ASBO) is a benign disease, the associated mortality is not null, and rates of up to 8% have been reported [1—4]. Furthermore, 5% of cases of ASBO constitute a medical emergency [5,6]. Likewise, the associated costs are not negligible (around $ 9,000 per case for non-surgical management and between $ 30,000 and 40,000 for surgery) [7].

In 2013, the management of uncomplicated ASBO was summarized in the ''Bologna Guidelines'' by the World Society of Emergency Surgery's working group on ASBO [8]. The management is based on monitoring the resolution of small bowel obstruction (i.e. the restoration of intestinal transit) or the appearance of signs that are suggestive of bowel damage (strangulation or peritonitis). Management is straightforward if signs of complications are present but is difficult if there are no signs of strangulation or peritonitis when intestinal transit has not been restored.

Soluble contrast medium (such as Gastrografin®) has been proposed as a diagnostic test for small bowel obstruction; if the contrast agent is observed in the caecum, intestinal transit has been restored. Gastrografin® also has a therapeutic effect via the stimulation of bowel peristalsis [9]. In two meta-analyses, Gastrografin® was found to reduce the surgery rate by 30% and reduce the length of hospital stay (LOS) by 1.87 days [9,10]. However, this trend was not confirmed by the recently published results of our randomized clinical trial (the ABOD study: NCT00389116). Pooling our data with those of the 2015 meta-analysis failed to reveal a benefit of Gastrografin® in terms of the surgery rate and the LOS [11,12].

Given the absence of a criterion for the failure of non-surgical management or for surgery as first-line treatment, biomarkers such as procalcitonin (PCT) have been investigated in the context of ASBO. PCT has been described as a marker of infection and inflammation and may help to identify: (i) ASBO patients with failure of non-surgical management, and (ii) those requiring surgery [13,14]. On the basis of the results of the latter two series, we developed a PCT-based algorithm for ASBO management support (Fig. 1).

Hence, the objective of the present study was to characterize the impact of combining a PCT-based algorithm with clinical signs on the management of ASBO.

Patients and methods

Design

We performed a pilot, retrospective, single-center ''before—after'' study of the patients' medical records. Patients with ASBO were identified by searching for the ICD-10 code K56.5 (''adhesion-related small bowel obstruction''). Management of ASBO was described for two consecutive periods — the ''before'' period (2007—2012) and the ''after'' period (2013—2016) that differed solely with respect to the use of a PCT-based algorithm. During the ''before'' period, patients with uncomplicated ASBO ($n = 93$, the Gastrografin® group) underwent a clinical examination and a Gastrografin® index without the PCT-based algorithm. The ASBO management was based on two aspects:

- the restoration of intestinal transit (the presence of gas and/or stools);
- the suspected presence of damage to the intestinal tract (strangulation or peritonitis).

During this period, some of these patients (60 patients) were included in ABOD study and benefit of a PCT assay within the framework of this protocol. Nevertheless, the value was not integrated into the patient management scheme as decisional boundaries were unknown at this time. The data obtained during this period were used to develop the algorithm.

During the ''after'' period (2013 to 2016), patients with uncomplicated ASBO ($n = 70$, the algorithm group) underwent a clinical examination (but not a Gastrografin® test) and were assessed with the PCT-based algorithm. Again, patient management was based on two aspects:

- the restoration of intestinal transit (the presence of gas and/or stools);
- the suspected presence of damage to the intestinal tract (strangulation or peritonitis).

During this period, the PCT-based algorithm was integrated into the patient management scheme. During both periods, clinical information (the presence of transit, suspected strangulation or peritonitis, etc.) was always given more weight than the results of the Gastrografin® test or the PCT assay — regardless of the latter's values or in case of discrepancies between the two.

Population

The main inclusion criterion (i.e. uncomplicated, acute ASBO) was defined as follows during both periods: SBO in the absence of fever, abdominal pain or distention, nausea and/or vomiting, no transit of gas and/or stools, and a contrast-enhanced CT scan in patients with previous abdominal surgery.

The exclusion criteria were as follows:

- large bowel obstruction, signs of peritonitis or strangulation (acute pain, hyperthermia and/or a white blood cell count above 16,000/mL);
- no previous abdominal surgery;
- obstruction in the 4 weeks following previous surgery;
- active or previous cancer of the intestinal tract;
- active or previous inflammatory bowel disease;
- a history of abdominal radiotherapy.

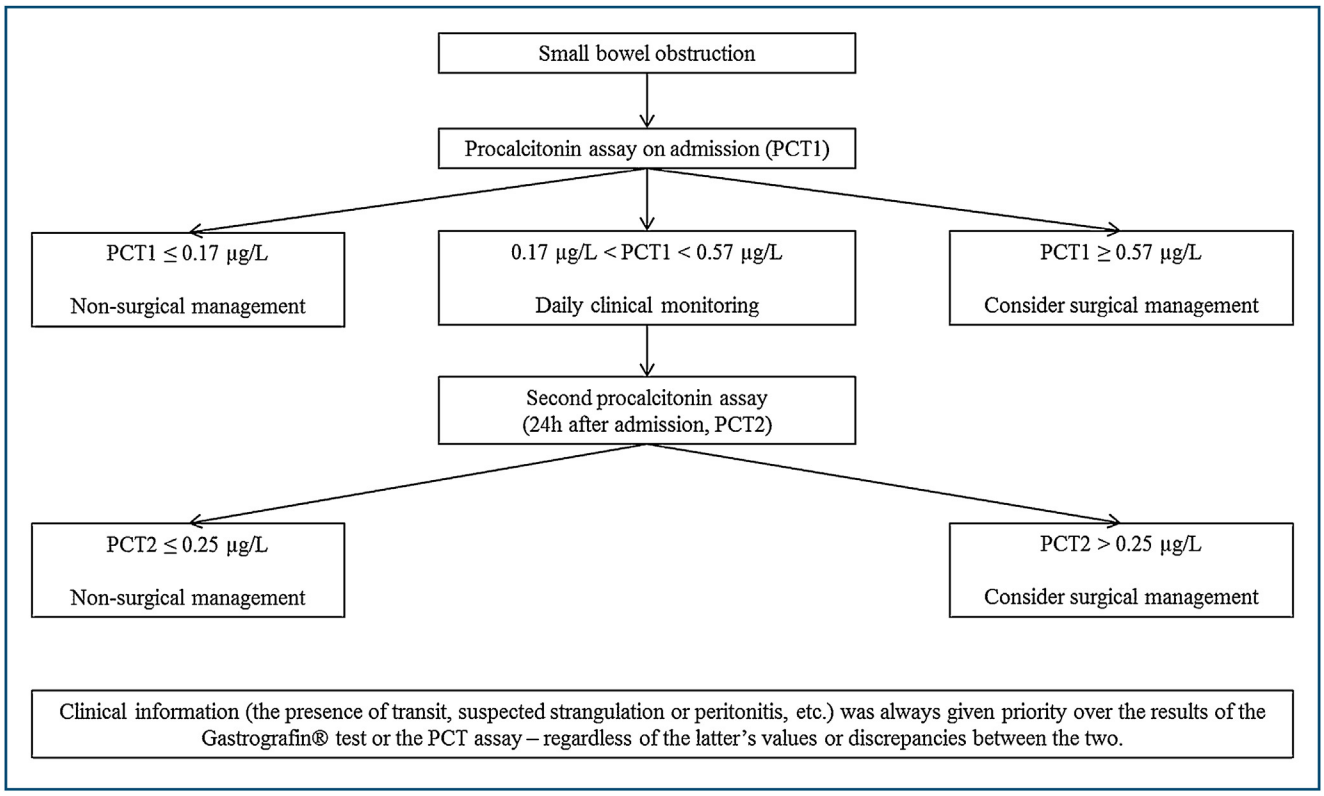

Figure 1. The procalcitonin-based algorithm.

Development of the PCT-based algorithm

On the basis of the data collected in the ABOD randomized clinical trial during the ''before'' period, we identified PCT as a valuable biomarker for patient management [11]. In a second cohort of patients, PCT levels were assayed every six hours for 3 days or until restoration of transit [12] in order to evaluate PCT's predictive time points and the associated threshold for the failure of non-surgical management. Thresholds with the highest diagnostic values (sensitivity, specificity and predictive values) were selected as boundaries for the success or failure of non-surgical management. The treatment algorithm was as follows:

- on admission, a PCT value $\leq 0.17\,\mu g/L$ indicates non-surgical management;
- a value $\geq 0.57\,\mu g/L$ indicates surgical management;
- a value between these two boundaries indicates the need to repeat the PCT assay 24 hours later.

Twenty-four hours after admission, a PCT value $\leq 0.25\,\mu g/L$ indicates the continuation of non-surgical management and a PCT value $\geq 0.25\,\mu g/L$ indicates the need for surgical management.

Study endpoints

The primary outcome was the appropriateness of the ASBO management (defined as the proportion of well-managed patients) in the two treatment periods. This proportion was calculated as follow: (number of patients in whom surgery was appropriate + number of patients in whom non-surgical treatment was appropriate)/the total number of patients. To be considered as getting an appropriate management, patients should not consult or be hospitalized for ASBO within the 90 days following the discharge. Patients should not consult at the emergency department, be hospitalized or operated on for symptoms related to ASBO and its management.

Secondary outcomes

The secondary outcomes were related to surgical management (the need for surgery, the time before surgery), the time to transit restoration, the LOS, the morbidity and mortality rates, the recurrence rate, and health economic data (PCT assay, days of nursing care, and days of hospitalization).

Management of uncomplicated ASBO

A nasogastric tube (NGT) with a negative pressure of 40 cm H_2O was inserted for aspiration of the upper digestive tract contents. The patient's electrolyte balance was restored or maintained intravenously during the aspiration. After two hours of aspiration, patients in the Gastrografin® group received 100 ml of Gastrografin®. The NGT was then clamped for the next two hours. If the patient vomited, the NGT was re-opened. If flatus was noted, the NGT was removed and oral refeeding (with water or with liquid food) was initiated.

The indications for surgery were based on the following: suspected ischemic damage to the digestive tract (acute pain, signs of strangulation, peritonitis, fever and/or a white blood cell count > 16,000/mL) and the absence of flatus or stools 48 hours after initiation of non-surgical management. The study flowchart is shown in Fig. 2.

Effective to enroll

As the proportion of appropriately managed patients is unknown in the literature, we proposed to base our hypothesis on the available data, i.e. the readmission rate within 90 days after the discharge [15,16]. We expected 30% of the

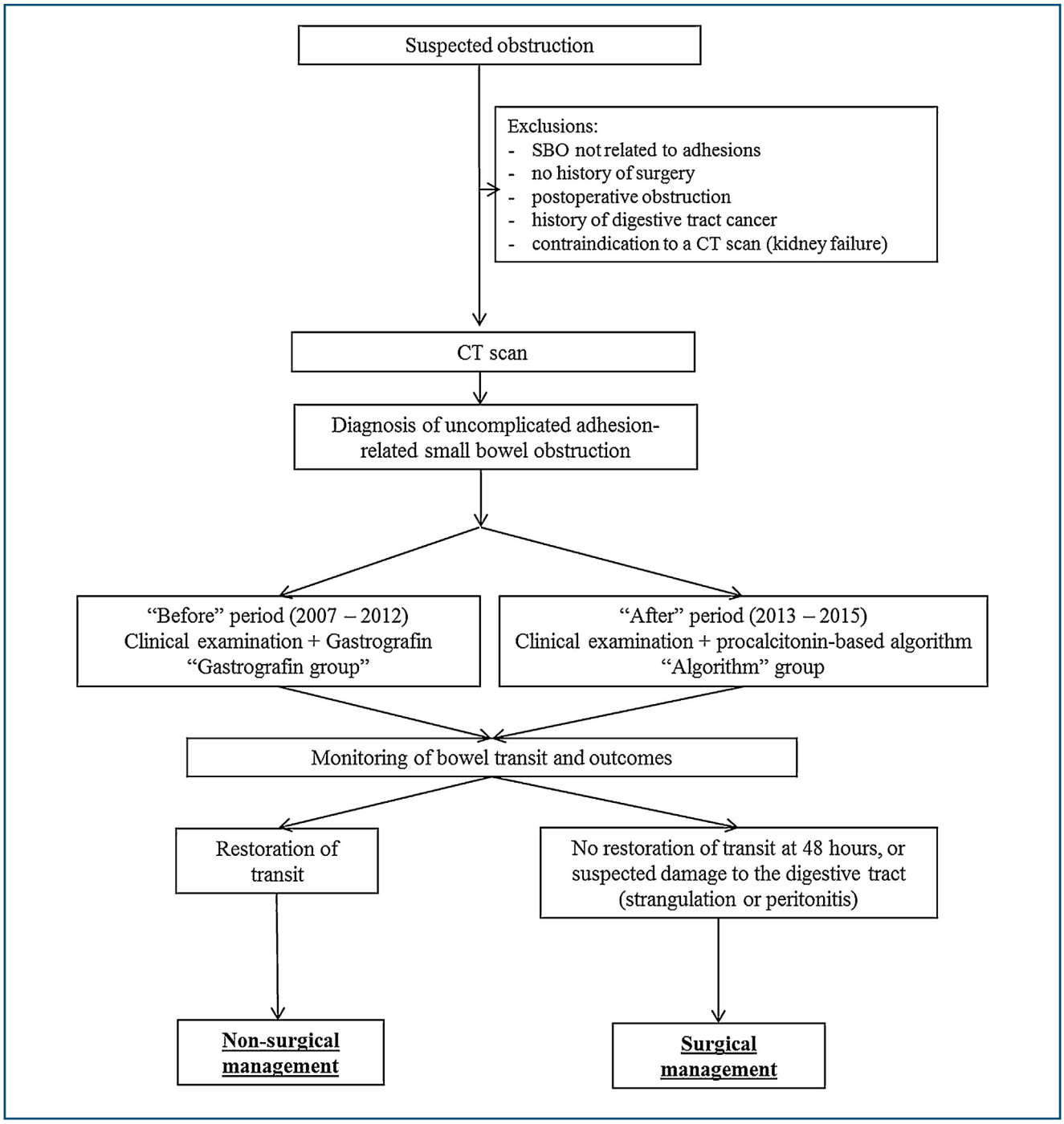

Figure 2. Study flowchart.

patients in the Gastrografin® group and 10% of the patients in the algorithm group to be readmitted within the 90 days after the discharge. Hence, in order to achieve a power of 80% and with an alpha risk of 5%, 140 patients had to be included.

Statistical analysis

Quantitative variables were expressed as the mean ± standard deviation (SD) or the median (range). Qualitative variables were expressed as the number (percentage). Univariate analyses were based on the t test (for quantitative variables) and the chi-squared test (for qualitative variables). For all analysis, a P value ≤ 0.05 was considered to be statistically significant. Statistical analysis was performed with SAS software (version 9.2; SAS Institute Inc., Cary, NC, USA) and PASW software (version 22, SPSS Inc., Chicago, IL, USA).

Results

Characteristics of the study population

The characteristics of the population are reported in Table 1. There were no significant differences between the two periods. In the algorithm group, the mean ± SD PCT value was 0.10 ± 0.06 μg/L at admission and 0.21 ± 0.13 μg/L 24 hours after admission.

Table 1 Characteristics of the study population.

Variables	Gastrografin® group $n=93$	Algorithm group $n=70$	*P* value
Male gender, *n* (%)	45 (48)	27 (39)	0.21
Age, mean ± SD	65 ± 19	66 ± 21	0.64
Cardiac comorbidity, *n* (%)	51 (55)	32 (46)	0.25
Respiratory comorbidity, *n* (%)	9 (10)	11 (16)	0.25
Renal comorbidity, *n* (%)	12 (13)	15 (21)	0.15
Neurologic comorbidity, *n* (%)	21 (23)	19 (27)	0.50
Appendectomy, *n* (%)	60 (65)	49 (70)	0.46

Appropriateness of management

The proportion of appropriately managed patients with ASBO was higher ($P<0.001$) in the algorithm group (86%, $n=60$ patients) than in the Gastrografin® group (47%, $n=43$ patients).

Surgery-related parameters

The data on surgery are reported in Table 2. The need for surgery was similar in the two periods (37% during the ''before'' period *vs.* 31% during the ''after'' period, $P=0.49$), whereas the time to surgery was shorter during the ''after'' period than during the ''before'' period (48 hours *vs.* 72 hours, respectively; $P=0.02$). The time to restoration of transit was similar in the two periods (53 hours during the ''before'' period and 41 hours during the ''after'' period; $P=0.11$).

Description of inappropriate management

Inappropriate management corresponds to patients who underwent surgery after initially being assigned to non-surgical management.

In the Gastrografin® group, 24 patients (26%) were considered to have undergone successful non-surgical management (visualization of Gastrografin® in the caecum), although no gas was observed and the patients experienced abdominal pain. The decision to operate was taken within the first 48 hours and, in most cases, consisted of adhesiolysis. In the algorithm group, 10 patients (14%) were operated after initial non-surgical management. The decision to operate was taken within the first 48 hours and, in most cases, consisted of adhesiolysis.

Postoperative data

The postoperative morbidity, mortality and recurrence rates were similar in the two periods and were the following (15% in the ''before'' period *vs.* 13% in the ''after'' period for morbidity, $P=0.69$; respectively 2% *vs.* 3% for mortality, $P=0.82$; respectively 10% *vs.* 7% for recurrence; $P=0.57$) (Table 2). The LOS was lower during the ''after'' period (4 [3—14] days) than during the ''before'' period (6 [2—26] days, $P=0.02$).

Economic data

Health economic data are reported in Table 3. The cost of the PCT assay was obviously higher in the second period (by € 30 per patient). The other costs were significantly higher during the first period than during the second period (respectively € 1920 *vs.* € 1280 for nursing care, $P=0.03$; € 2400 *vs.* € 1600 for hospitalization, $P=0.02$).

Discussion

The present study was designed to evaluate the clinical and health economic impact of a PCT-based algorithm for the management of ASBO. We found that during the ''after'' period (i.e. following the inclusion of the PCT-based algorithm in the decision tree), the management of ASBO was more accurate, the time to surgery was shorter (by 24 hours), the LOS was shorter (by 2 days), and there was no increase in the surgery rate.

This series is the first to have evaluated the impact of a biomarker (PCT) and clinical examination on the ASBO management process. Moreover, the benefit of the algorithm for PCT (a biomarker that can now be routinely assayed in

Table 2 Surgery-related parameters.

Variable	Gastrografin® group $n=93$	Algorithm group $n=70$	*P* value
Appropriateness of management	43 (47)	60 (86)	< 0.001
Time to restoration of transit, h, mean ± SD	53 ± 6	41 ± 9	0.11
Proportion of operated patients, *n* (%)	34 (37)	22 (31)	0.49
Time to surgery, h, mean ± SD	72 ± 5	48 ± 8	0.02
Mortality rate, *n* (%)	2 (2)	2 (3)	0.82
Length of stay, days, median (min—max)	6 (2—26)	4 (3—14)	0.02
Recurrence rate, *n* (%)	9 (10)	5 (7)	0.57

Table 3 Health economic data.

Variable	Gastrografin® group $n = 93$	Algorithm group $n = 70$	*P* value
PCT assay, €, median	0	30	0.01
Days of nursing care, €, median	1920	1280	0.03
Days of hospitalization, €, median	2400	1600	0.02

all biochemistry laboratories) in terms of the LOS and the time to restoration transit did not come at the expense of an increase in the need for surgery. This might have been due to more accurate selection of patients for monitoring. Furthermore, the shorter LOS and the shorter time to restoration of transit might have been due to the fact that physician is more proactive when all the indicators are positive (increased mobilization, early removal of NGT, early oral refeeding, and early discharge). These items have been integrated into the concept of ''enhanced recovery'', which was first described by Kehlet as a means of reducing postoperative morbimortality and undesirable sequelae after surgery [17—19]. Since Kehlet's proposal, many articles on this topic have been performed in various fields of surgery (e.g. digestive, gynecological and orthopedic surgery) [20]. Moreover, enhanced recovery is now being applied to oncological surgery and emergency surgery (perforated peptic ulcer, obstructing colorectal cancer, etc.) [21,22]. Thus, the impact of a PCT-based algorithm on patient management may contribute to propose enhanced recovery in ASBO.

The PCT-based algorithm is of clinical interest because there are no other alternatives to the Gastrografin® test. Our recent ABOD randomized clinical trial evaluated the surgery rate associated with Gastrografin® vs. saline tests [12]. No benefit of Gastrografin® was seen. To put the results into perspective the data from the ABOD study ($n = 242$) was pooled with the data included in the latest meta-analysis ($n = 990$) [11]. The results confirmed that Gastrografin® was of no benefit with regard to the surgery rate and the LOS. Hence, the Gastrografin® test is not yet of value in routine practice.

The present series had several limitations. Firstly, its retrospective design may have contributed to a lack of data. Secondly, the fact that the data came from a single center means that the results from the ''after'' period could have been modified by the addition of the PCT assay to the clinical decision tree. Nevertheless, the present series is the largest yet assessment of biomarker use in the management of ASBO.

In the context of enhanced post-surgery recovery, biomarkers may be of value but need to be investigated in very large cohorts. To this end, we intend to organize a prospective, randomized clinical trial of the algorithm's impact on the success rate in ASBO management.

Conclusion

The use of a PCT-based algorithm is of value in the routine clinical management of ASBO; it reduces the LOS and the time to surgery without increasing the need for surgery.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Zalcman M, Sy M, Donckier V, Closset J, Gansbeke DV. Helical CT signs in the diagnosis of intestinal ischemia in small-bowel obstruction. AJR Am J Roentgenol 2000;175(6):1601—7.
[2] Rubesin SE, Herlinger H. CT evaluation of bowel obstruction: a landmark article-implications for the future. Radiology 1991;180(2):307—8.
[3] Deshmukh SD, Shin DS, Willmann JK, Rosenberg J, Shin L, Jeffrey RB. Non-emergency small bowel obstruction: assessment of CT findings that predict need for surgery. Eur Radiol 2011;21(5):982—6.
[4] Frager DH, Baer JW. Role of CT in evaluating patients with small-bowel obstruction. Semin Ultrasound CT MR 1995;16(2):127—40.
[5] Shatila AH, Chamberlain BE, Webb WR. Current status of diagnosis and management of strangulation obstruction of the small bowel. Am J Surg 1976;132(3):299—303.
[6] Bevan PG. Adhesive obstruction. Ann R Coll Surg Engl 1984;66(3):164—9.
[7] Bilderback PA, Massman JD 3rd, Smith RK, La Selva D, Helton WS. Small bowel obstruction is a surgical disease: patients with adhesive small bowel obstruction requiring operation have more cost-effective care when admitted to a surgical service. J Am Coll Surg 2015;221(1):7—13.
[8] Di Saverio S, Coccolini F, Galati M, et al. Bologna guidelines for diagnosis and management of adhesive small bowel obstruction (ASBO): 2013 update of the evidence-based guidelines from the world society of emergency surgery ASBO working group. World J Emerg Surg 2013;8(1):42.
[9] Abbas SM, Bissett IP, Parry BR. Meta-analysis of oral water-soluble contrast agent in the management of adhesive small bowel obstruction. Br J Surg 2007;94(4):404—11.
[10] Branco BC, Barmparas G, Schnüriger B, Inaba K, Chan LS, Demetriades D. Systematic review and meta-analysis of the diagnostic and therapeutic role of water-soluble contrast agent in adhesive small bowel obstruction. Br J Surg 2010;97(4):470—8.
[11] Ceresoli M, Coccolini F, Catena F, et al. Water-soluble contrast agent in adhesive small bowel obstruction: a systematic review and meta-analysis of diagnostic and therapeutic value. Am J Surg 2016;211(6):1114—25.
[12] Scotte M, Mauvais F, Bubenheim M, et al. Does the use of water-soluble contrast medium (gastrografin) reduce the need for surgery and the length of stay in uncomplicated acute adhesion-related small bowel obstruction? A multicenter, randomized, clinical trial and systematic review. Surgery 2017.
[13] Cosse C, Regimbeau JM, Fuks D, Mauvais F, Scotte M. Serum procalcitonin for predicting the failure of conservative management and the need for bowel resection in patients with small bowel obstruction. J Am Coll Surg 2013;216(5):997—1004.
[14] Cosse C, Sabbagh C, Rebibo L, et al. Kinetics of procalcitonin in the management of small bowel obstruction: a preliminary report. Surgery Curr Res 2014:184.
[15] Bardram L, Funch-Jensen P, Jensen P, Crawford ME, Kehlet H. Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation. Lancet 1995;345(8952):763—4.

[16] Miller G, Boman J, Shrier I, Gordon PH. Natural history of patients with adhesive small bowel obstruction. Br J Surg 2000;87(9):1240—7.
[17] Williams SB, Greenspon J, Young HA, Orkin BA. Small bowel obstruction: conservative vs. surgical management. Dis Colon Rectum 2005;48(6):1140—6.
[18] Kehlet H. Organizing postoperative accelerated recovery programs. Reg Anesth 1996;21(6 Suppl.):149—51.
[19] Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth 1997;78(5): 606—17.
[20] Gonenc M, Dural AC, Celik F, et al. Enhanced postoperative recovery pathways in emergency surgery: a randomized controlled clinical trial. Am J Surg 2014;207(6):807—14.
[21] Lohsiriwat V. Enhanced recovery after surgery vs. conventional care in emergency colorectal surgery. World J Gastroenterol 2014;20(38):13950—5.
[22] Simpson JC, Moonesinghe SR, Grocott MP, et al. National Enhanced Recovery Partnership Advisory Board. Enhanced recovery from surgery in the UK: an audit of the enhanced recovery partnership programme 2009-2012. Br J Anaesth 2015;115(4):560—8.