

PROCOLE (Prognostic Colorectal Leakage): A New Prognostic Index to Predict the Risk of Anastomotic Leak in Colorectal Cancer Surgery

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Abstract

Objective: To develop a prognostic index to predict the risk of developing anastomotic leakage after colorectal cancer surgery, this has been named PROCOLE (prognostic colorectal leakage).

Methods: A systematic review of the literature of observational studies has been performed to identify risk factors and then, a meta-analysis of each factor has been done. The factors that are statistically significant are weighted according to the value of the effect size. The prognostic index has been validated by an observational, longitudinal, retrospective, case-control data collection.

Results: The predictive ability of the PROCOLE is made from the data obtained from the sample of cases and controls, resulting in an area under the curve (AUC) of 0.82 with a confidence interval of 95% of the AUC [0.75, 0.89].

Conclusions: The PROCOLE score predicts the risk of developing anastomotic leakage and may be useful to assist operative decision-making such as the implementation of a protective stoma.

Keywords: Anastomotic leakage, Colorectal surgery, Risk factors, Meta-analysis, Prognostic index.

Introduction

Anastomotic leak is recognized as the leading cause of morbidity and mortality in colorectal cancer surgery and is associated with a significant increase in the length of hospital stay. The main difficulty in predicting the risk of anastomotic leakage is its aetiology which includes a large number of related risk factors, and it is reflected in the very poor predictive ability of surgeons to identify which patients may develop a leak [1]. An additional difficulty is that the anastomotic leakage lacks a universally accepted definition and objectives comparisons between different studies are impossible [2-3]. There is a need to obtain better prognostic criteria that can assist operative decision-making, [4], because there is a proposal for the application of a protective stoma, called colon leakage score (CLS) but it needs to be validated with different samples [5].

Methods

The methodological sequence [6] consists of the six following stages (Figure 1):

Basic search of the literature (Ovid-MEDLINE database) published in English between 2002 and 2012 and systematic review with identification of the potential risk factors for anastomotic leakage [7-56]. The publications are filtered, selecting those in which the abstract describes at least one risk factor. The bibliography used on these articles was also considered. Result: 151 publications.

Selection of the publications containing enough information for completing a contingency table with the occurrence of anastomotic leak and the risk factor. Result: 68 publications. Meta-analysis of each risk factor is done. The effect size is represented using the odds ratio (OR).

Only those risk factors in which the meta-analysis reached statistical significance for a confidence interval of 95% of the OR are included. The weight assigned to each factor corresponds to the natural logarithm of the estimated result of a corresponding OR meta-analysis. To the prognostic index, has been termed PROCOLE (Prognostic colorectal leakage).

The prognostic index has been validated by an observational, longitudinal, retrospective, case-control data collection. The sample consists of 41 cases (patients who developed an anastomotic leak) and 82 (patients who did not develop an anastomotic leak) controls randomly selected from the population of patients undergoing surgery for colorectal cancer in the Coloproctology Unit of the General Surgery Department of the University Hospital of Alicante in the time interval between May 1, 2003 and May 31, 2010.

This validation is performed by calculating the area under the curve (AUC) of the receiver operating characteristic (ROC).

The selection threshold is identified from the prognostic index. This enables de recommendation on whether to protect the stoma based on the sensitivity and specificity curves.

Results

A total of 54 potential risk factors were found from the initial basic search of the 68 publications that were useful. A meta-analysis was performed, taking into account 48 out of the 54 risk factors. Statistical significance was found in 27 of the 48 meta-analysed factors for a 95% confidence interval of the OR (Figure 2).

The preoperative risk factors are: drug abuse (alcohol and/or tobacco; OR=1.49, 95% confidence interval (CI) of the OR=1.14, 1.94), cardiovascular diseases (OR=1.30, 95% CI of the OR= 1.03, 1.64), diabetes mellitus (OR=1.60, 95% CI of the OR=1.12, 2.13), renal pathology (OR=1.56, 95% CI of the OR=1.23, 1.99), respiratory disease (OR=1.89, 95% CI of the OR=1.37, 2.61), hepatic pathology (OR=1.79, 95% CI of the OR=1.35, 2.38), simultaneous diseases (OR=2.54, 95% CI of the OR=1.25, 5.13), male gender (OR=1.51, 95% CI of the OR=1.63, 1.69), ASA higher to 3 (OR=1.76, 95% CI of the OR=1.39, 2.23), obesity (OR=1.68, 95% CI of the OR=1.33, 2.12), preoperative levels of albumin <3.5 g/dl (OR=2.70, 95% CI of the OR=2.01, 3.62), neoadjuvant therapy (OR=1.61, 95% CI of the OR=1.23, 2.09), steroid consumption (OR=2.02, 95% CI of the OR=1.21, 3.36). The operative risk factors are: emergency surgery (OR=1.96, 95% CI of the OR=1.49, 2.59), additional surgery (OR=1.74, 95% CI of the OR=1.09, 2.79), mechanical anastomosis (OR=1.21, 95% CI of the OR=1.04, 1.41), intraoperative blood transfusion (OR=2.26, 95% CI of the OR=1.65, 3.07), intraoperative adverse event (OR=2.96, 95% CI of the OR=2.00, 4.37).

Cardiovascular diseases	0.26
Respiratory diseases	0.64
Renal pathology	0.45
Hepatic pathology	0.58
Concurrency presented pathologies	0.93
Male sex	0.41
Obesity (IMC >30 kg/m2)	0.52
Classification ASA ≥ 3	0.57
Steroids consumption	0.70
Neoadjuvant treatment	0.47
Preoperative albumin levels <3.5 g/dl	0.99
Emergency surgery	0.67
Additional surgery simultaneous to colorectal surgery	0.55
Mechanical anastomosis	0.19
Intraoperative blood transfusion	0.81
Intraoperative adverse event that the primary surgeon considered as such and reflects on the part of theater	1.08

Table 1: Weight of the factors for the calculation of the prognostic index of anastomotic leak in colorectal cancer surgery PROCOLE (PROgnostic COlorectal LEakage).

The variables considered in terms of historic results are the anastomotic leak incidence of the surgeon and the duration of the surgery. The appropriate score of the type of surgery is shown in Table 2.

Factor	Weight (β)
Intraperitoneal resection: high anterior resection (anastomosis placed more than 10 cm far from the anal verge), right hemicolectomy, high left segmentary colectomy, left hemicolectomy, transverse hemicolectomies, sigmoidectomy and subtotal colectomy	0
Low anterior resection (anastomosis placed less than 5 cm from the anal verge)	0.82
Ultralow anterior resection (anastomosis placed between 5 cm and 10 cm from the anal verge)	1.64

Table 2: Weight of the factor concerning the type of surgical intervention in colorectal cancer for the calculation of the prognostic index of anastomotic leak PROCOLE (PROgnostic COlorectal LEakage).

The prognostic index, denominated PROCOLE (prognostic colorectal leakage) is calculated in a specific patient as follows:

PROCOLE value=Total (summation) of the weights (scores) of the present factors in Table 1+type of intervention (surgery) score present in Table 2+duration score.

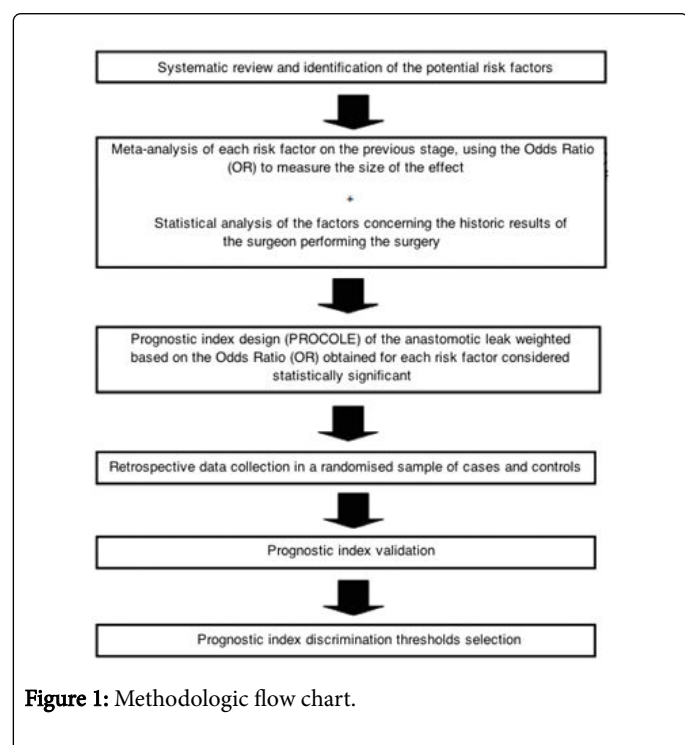
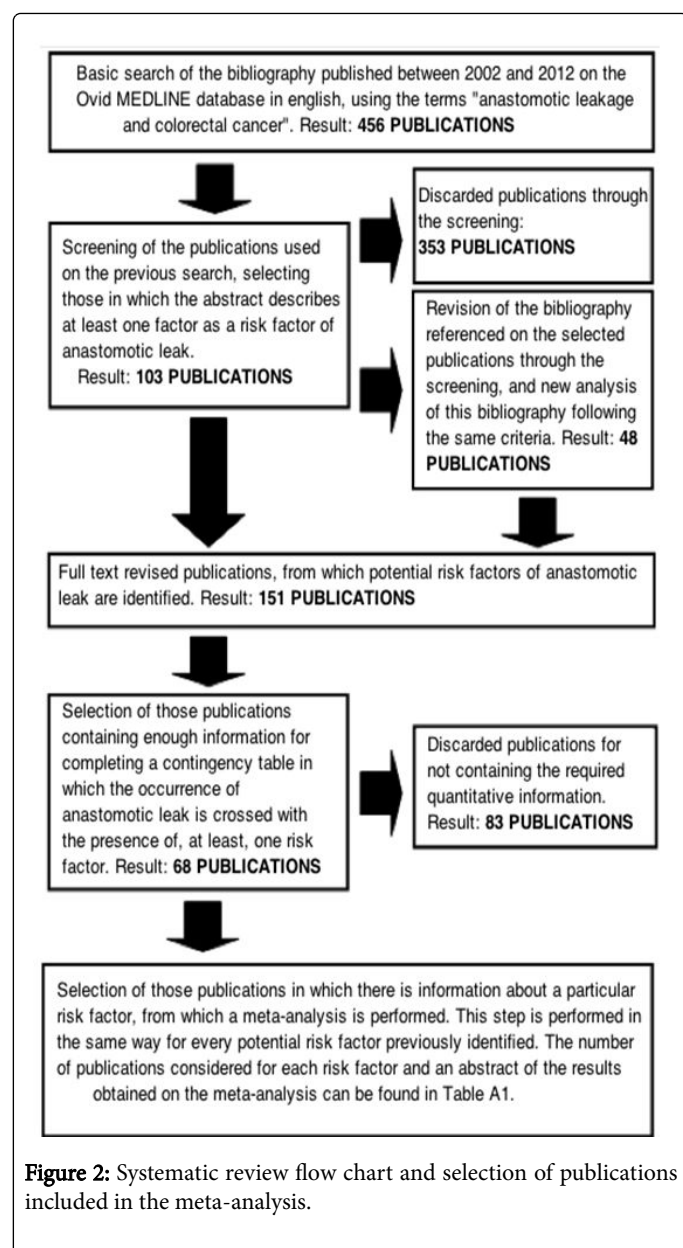


Figure 1: Methodologic flow chart.

The weight assigned (score) to each factor corresponds to the natural logarithm of the estimated result of a corresponding OR meta-analysis. The scores are shown in Table 1.

Factor	Weight (β)
Drugs consumption (alcohol and / or tobacco)	0.40
Diabetes mellitus	0.47



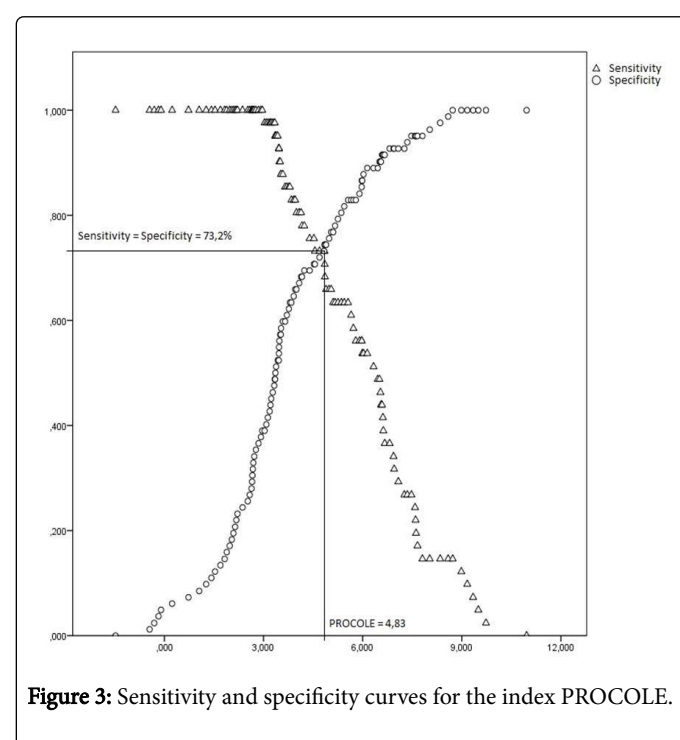
The assessment of the predictive ability of the prognostic index PROCOLE is made from the data obtained from the sample of cases and controls, resulting in an AUC of 0.82 with a standard error of 0.04 and a confidence interval of 95% AUC [0.75, 0.89]. As such, it can be considered a good prognostic indicator.

Discussion

The new prognostic index can be used to predict the risk of a certain individual developing anastomotic leakage after colorectal cancer surgery. PROCOLE establishes a discrimination value threshold of 4.83 for recommending the implementation of a protective stoma. It should also be noted that the studies that integrate the meta-analysis have not been limited with a superior evidence level finally demanded because the strategy followed have been to sacrifice quality to number, this is a limitation of this study.

A similar index called colon leakage score (CLS) already exists [5], but its predictive power is lower than that estimated for the PROCOLE index. When its predictive capacity is tested using a cases and controls sample, the estimated area under the curve for the CLS is 0.65, with a confidence interval of 95% [0.55, 0.75].

This study could be furthered in three aspects. The first is the refinement of the PROCOLE index by extending the meta-analysis of each of the factors. However, it must be noted that since these factors are cumulative in nature, new factors may be identified in future studies. The second aspect is to carry out a prospective study on the clinical application of the protocols. Finally, the third is the refinement of the PROCOLE index in order to predict the occurrence of anastomotic leak, as well as to determine its severity (Grade A, B or C). Additionally, the index may also be exposed to critical examination by other researchers (Figure 3).



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