

LAR vs VLAR in Low Rectal Cancer - Postoperative Results - A Single-Center Experience

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Rezumat

RAJ vs RAFJ în cancerul rectal jos situat - rezultate postoperatorii - experiența unui singur centru

Introducere: Managementul terapeutic al cancerului rectal recunoaște rezecția chirurgicală ca fiind pasul cel mai important pentru obținerea vindecării. Respectând principiile oncologice, prezervarea funcțională reprezintă o prioritate pentru atingerea unei calități acceptabile a vieții acestor pacienți. Acest studiu își propune să compare rezultatele postoperatorii după rezecția rectală anterioară joasă (RAJ) cu cele după rezecția anterioară foarte joasă (RAFJ).

Material și metodă: Am realizat un studiu retrospectiv, observațional ce a inclus 147 de pacienți cu RAJ sau RAFJ realizate pentru cancere rectale joase în Clinica Chirurgie I a Spitalului Clinic Județean de Urgență Târgu Mureș, între ianuarie 2015 și decembrie 2019. Am considerat ca fiind cancere rectale joase acele tumori localizate între 5-10 cm de la marginea anală și foarte joase pe acelea situate sub 5 cm față de aceasta. Pacienții au fost împărțiți în două grupuri în funcție de tipul operației efectuate. Au fost urmărite rezultatele postoperatorii.

Rezultate: Cele două grupuri, RAJ cu 81 și RAFJ cu 66 de cazuri, au înregistrat o distribuție omogenă a parametrilor demografici și biologici și a caracteristicilor tumorale. O durată semnificativ mai mare ($p = 0,0223$) a intervenției chirurgicale s-a înregistrat în grupul cu RAFJ comparativ cu RAJ. Nu s-au identificat diferențe semnificative statistice între cele două grupuri privind morbiditatea și mortalitatea postoperatorie și nici durata de spitalizare.

Concluzii: Nu au fost diferențe statistice între rezultatele post-

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operatorii precoce obținute în grupurile RAJ și RAFJ. Cel mai important factor pentru obținerea unor bune rezultate oncologice și funcționale, în tratamentul cancerelor rectale joase este alegerea unui management chirurgical adecvat, individualizat, pentru fiecare pacient.

Cuvinte cheie: cancer rectal jos, prezervare sfincteriană, rezecție rectală anterioară joasă, rezecție rectală anterioară foarte joasă

Abstract

Background: The management of rectal cancer recognizes surgical resection as the most important step towards a permanent cure. Respecting the oncological principles, functional preservation represents a priority in achieving an acceptable quality of life for the patient. This study aimed to compare the results after low anterior resection (LAR) versus very low anterior resection (VLAR), in terms of postoperative outcome.

Methods: We conducted a retrospective, observational study on a group of 147 patients with LAR or VLAR done for low rectal cancer in the 1st Department of General Surgery of the Emergency County Hospital of Targu Mures, between January 2015 and December 2019. We considered as low rectal cancer tumors located between 5-10 cm from the anal verge and very low those situated less than 5 cm from it. Patients were divided in two groups according to the type of operation. The post-operative evolution was followed.

Results: The two groups, LAR with 81 and VLAR with 66 cases, had homogenous distribution regarding patients' demographic and biological parameters and tumor pathological features. A significantly ($p=0.0223$) longer surgical intervention time was reported in VLAR than in LAR procedures. We found no statistically significant differences between LAR and VLAR in terms of associated postoperative morbidity or mortality, neither in hospitalization time.

Conclusions: There was no statistical difference in terms of early postoperative outcomes among LAR and VLAR. The most important factor in achieving good oncologic and functional results in low rectal cancer is choosing the adequate, tailored to the case surgical management.

Key words: low rectal cancer, sphincter-saving procedure, low anterior rectal resection, very low anterior rectal resection

Introduction

Colorectal cancer is the first among the digestive sites and the third most common cancer worldwide. It represents also the second leading cause of cancer death in the world (1).

The modern management of rectal cancer, nowadays, recognizes a multimodal approach that combines surgical resection, regional radiation therapy, and chemotherapy (2,3).

The surgical treatment of rectal cancer, in accordance with technological advances and a better understanding of the disease behavior, recognizes a continuous evolution in developing

surgical techniques aiming to improve not only the oncological results but also the quality of life for the patients. (4)

The concept of total mesorectal excision and the use of preoperative chemoradiotherapy leading to low local recurrence rates (5-8), along with the decrease of the distal safety margin, to less than 1 cm (4,5), caused an increase in sphincter preserving surgery rate and a fall in the use of abdominoperineal excision (5,9,10).

Throughout time, in our surgical department a particular interest has been developed concerning the treatment of colorectal pathology and especially of low and very low rectal

cancers. The main challenge was to try to pursue the aim of functional preservation, respecting also the gold standard oncological rules. This activity constantly tried to keep up to date with all the scientific evolution in the field, practicing, over time, a wide range of sphincter-saving techniques, adapted as an indication to each patient.

This study aimed to compare the results of low anterior resection (LAR) versus those after very low anterior resection (VLAR) performed, in the last five years, in the 1st Department of General Surgery, in patients with low rectal cancers, in terms of postoperative outcome.

Material and Methods

We conducted a retrospective, observational, and descriptive study on a group of 285 patients hospitalized and surgically treated for low rectal cancer in the 1st Department of General Surgery of the Emergency County Hospital of Targu Mures, over the recent 5 years (between January 2015 and December 2019).

We considered as low rectal cancer tumors located between 5-10 cm from the anal verge and very low those situated less than 5 cm from it.

The study included patients that underwent a rectal resection, within oncological principles, followed by a primary anastomosis for pathologically confirmed low rectal cancer. We excluded patients to whom no rectal resection was made, but other palliative or diagnostic procedures, those for which the rectal resection was not completed with an anastomosis or was done for a benign disease. We excluded also the patients with intersphincteric resection (ISR) and other procto-recto-colectomy with coloanal anastomosis.

Patients were divided in two groups according to the type of operation they underwent:

- Group I - patients with low anterior rectal resection (LAR).
- Group II - patients with very low anterior rectal resection (VLAR).

The objective of the study was to evaluate the therapeutic option (surgical procedure)

and to follow the postoperative evolution (in terms of operative time, postoperative complications, mortality, length of stay in hospital) in correlation with the demographic and biological parameters of the patients, the tumor clinical and pathological features (histological grade, TNM staging, vascular, lymphatic and perineural invasion) and the associated oncological treatment.

The evaluation of the cases was conducted by assessing the physical, imaging, and laboratory examination data, the operative protocols, and the pathological results collected from the written and electronic database of the 1st Department of General Surgery and the Department of Pathology of the Emergency County Hospital of Targu Mures.

Statistical Analysis

Data were processed in Microsoft Excel, and statistical analysis was performed using Graph Pad Prism 6. We used statistical methods such as descriptive and analytic-inferential methods. We used Student test to evaluate the differences between the means of continuous variables in two groups and the ANOVA test to evaluate the differences between the means of continuous variables in four groups (expressed by mean \pm SD). A χ^2 test was used for categorical variables (expressed by numbers and percentages). The differences between continuous variables with non-normal distributions (expressed by median, range), were compared using the Mann-Whitney U test, respectively the Kruskal Wallis test. All the tests we have performed to materiality $p = 0.05$ and statistical significance was considered for p values less than the threshold value of significance.

Results

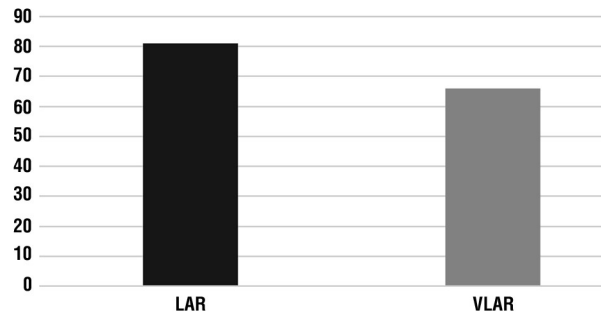
From the total number of 285 patients we excluded 10 inoperable cases, 63 patients to whom an ISR procedure was done and 65 cases with other procto-recto-colectomy with coloanal anastomosis or with abdomino-perineal resection - Miles procedure (APR).

The 147 (n = 147) cases registered in the study were distributed in two groups based on the type of surgical procedure: LAR with 81 cases (55.10%) and VLAR with 66 cases (44.90%) (Table 1, Graph 1).

The age of the patients ranged from 42 to 83 years, with an average of 71 years. We observed a male predominance with 99 cases (67%). The majority of the procedures were conducted as elective surgery. No statistically significant differences were observed between procedures regarding age, gender and type of surgery performed: as elective or emergency (Table 1).

Regarding local tumor complications, the most encountered was stenosis within 40 cases, predominant in LAR procedures (35.80%) with a significant statistical value (p=0.0148). Hemorrhage was present in 24 cases with no statistical difference between groups. Intraoperative exploration revealed tumor penetration in 19 cases involving the following organs: urinary bladder, seminal vesicles, prostate and uterus. Liver metastasis were present in 8 cases within LAR and 4 in VLAR group, with no statistical difference between them (Table 2).

Postoperative histopathological analysis of the resected tumors revealed that the most



Graph 1. Number of surgical procedures LAR/VLAR

encounter type was rectal adenocarcinoma with mucinous, micropapillary, and undifferentiated subtypes. Tumor grading (G) evaluation showed a predominance of G3 - high grade present in 58 cases with no statistically significant difference between the groups. Histopathological invasion characteristics were present at the vascular, lymphatic, and perineural levels with no significant differences (Table 3).

World Health Organization (WHO) Classification of Tumors of the colon and rectum 4th edition was used for the TNM classification of the tumors. The majority of the tumors were graded as T2 with 59 cases. Lymph node metastasis was predominantly

Table 1. Demographic characteristics and surgical approach

Procedures	Total	LAR	VLAR	p value
Cases	147	81	66	
Age (years) (mean ± SD)	71±7.3	70±3.5	71±11.2	0.1385*
Gender M	99	51	48	0.2092**
F	48	30	18	
Elective Surgery	139	75	64	0.2995 **
Emergency Surgery	8	6	2	

* Mann-Whitney U test, ** χ^2 test

Table 2. Local and systemic tumor complications

Procedures	Total	LAR	VLAR	p value
Stenosis (yes/no)	40/107	29/52	11/55	0.0148 *
Hemorrhage (yes/no)	24/123	16/65	8/58	0.2646*
Penetration (n=18/147)		(n=9/81)	(n=9/66)	
Urinary bladder (yes/no)	13/134	5/76	8/58	0.2498*
Seminal vesicles (yes/no)	3/144	2/79	1/65	1.0000*
Prostate (yes/no)	1/146	1/80	0/66	-
Uterus (yes/no)	1/146	1/80	0/66	-
Metastasis Hepatic (yes/no)	12/135	8/73	4/62	0.5481*

* χ^2 test

Table 3. Histopathological diagnosis

Procedures	Total	LAR	VLAR	p value
Adenocarcinoma	(n=138)	(n=74)	(n=64)	0.1870*
Mucinous	88	40	48	
Micropapillary	38	24	14	
Undifferentiated	12	10	2	
Carcinoma	(n=9)	(n=7)	(n=2)	0.1870*
Squamous	7	5	2	
Neuroendocrine	2	2	0	
Grading	(n=147)	(n=81)	(n=66)	0.8909**
G1	18	10	8	
G2	25	12	13	
G3	58	33	25	
G4	46	26	20	
Invasion	(n=29/147)	(n=21/81)	(n=8/66)	
Vascular (yes/no)	2/145	2/79	0/66	-
Lymphatic (yes/no)	15/132	12/69	3/63	0.0546**
Perineural (yes/no)	6/137	2/79	4/58	0.4032**
Peritumoral(yes/no)	6/141	5/76	1/65	0.2239**

World Health Organization (WHO) Classification of Tumors of the colon and rectum 4th edition* Fisher's exact test ** χ^2 test

present in 2-3 regional lymph nodes and structures near the lymph nodes (N1b-N1c). Metastasis was confined to one organ (M1a) in all 12 confirmed cases. Based on TNM staging the Dukes-Mac classification revealed a predominant A staging for the tumors with 43 cases (Table 4).

Preoperative oncological treatment consisted of radiotherapy, combined chemo-radiotherapy

or, in 25 cases, only chemotherapy. Preoperative tumor irradiation was performed in 49% of the patients, with a significant predominance in the LAR group procedures ($p=0.0201$). Adjuvant chemotherapy combined with radiotherapy was administered in 17% of the cases (Table 5).

Average surgical intervention time, for all procedures, was of 143 minutes. A significantly longer duration was reported in the VLAR than

Table 4. TNM and Dukes MAC staging

Procedures	Total	LAR	VLAR	p value
** TNM	(n=147)	(n=81)	(n=66)	-
T0	0	0	0	0.8571*
T1	45	25	20	1.0000*
T2	59	33	26	1.0000*
T3	38	20	18	1.0000*
T4a	5	3	2	-
T4b	0	0	0	-
N0	43	24	19	1.0000*
N1a	23	16	7	0.2458*
N1b	31	15	16	0.4225*
N1c	30	17	13	1.0000*
N2a	14	5	9	0.1608*
N2b	6	4	2	0.6911*
M0	135	73	62	0.5481*
M1a	12	8	4	0.5481*
M1b	0	0	0	-
M1c	0	0	0	-
***Dukes-Mac	(n=147)	(n=81)	(n=66)	
A	43	24	19	1.0000*
B	30	17	13	1.0000*
C	24	15	9	0.5043*
D	6	4	2	0.6911*

* χ^2 test**World Health Organization (WHO) Classification of Tumors of the colon and rectum 4th edition

*** ACJ Classification of Colorectal Tumors-Dukes-Mac Classification

Table 5. Preoperative oncological treatment

Procedures	Total	LAR	VLAR	p value
Radiotherapy (yes/no)	72/75	47/34	25/41	0.0201*
Chemo-radiotherapy (yes/no)	25/122	15/66	10/56	0.6625*
Chemotherapy (yes/no)	25/122	15/66	10/56	0.6625*

* χ^2 test

in LAR procedures, with an average time of 165 minutes, compared to 120 minutes ($p=0.0223$) (Table 6).

Average hospitalization time was of 17 days, with the shortest of 9 days and the longest of 38 days. There were no significant differences between the procedures regarding hospitalization time. The mortality rate was low in both groups, with no major difference between the procedures (Table 6).

The majority of the cases were treated with an open approach. Only 23 cases (15.64%) were operated laparoscopically, with 9 cases requiring conversion to a classic approach. There is no statistical difference between the two groups regarding the surgical approach and conversion rate (Table 7).

Regarding intraoperative management of

liver metastasis (M1a), in the 12 cases reported, only in five patients the metastases were completely resected (Table 8).

A total of 35 protective stomas were made, with no significant statistical difference between the two groups of procedures (Table 8).

Postoperative complications were encountered in all procedures. They were represented by anastomotic fistula, hemorrhage/hematoma, wound infection and evisceration. Wound infection was the most encountered within 24% of the total cases. Anastomotic fistula was developed the in 27 patients (18.36%). No statistically significant difference was reported between the groups regarding the distribution of postoperative complications (Table 9, Graph 2).

Regarding fistula cases, in both groups, the

Table 6. Operation time, hospitalization and mortality rate

Procedures	Total	LAR	VLAR	p value
Average operation time (min) (mean \pm SD)	143 \pm 6.3	120 \pm 8.5	165 \pm 1 0.5	0.0223*
Hospitalization time (days) (mean \pm SD)	17 \pm 1.7	19 \pm 2	15 \pm 1.5	0.6911*
Mortality	6 (4.08%)	4 (4.93%)	2 (3.03%)	0.6911**

*Mann-Whitney U test; ** χ^2 test

Table 7. Type of surgical approach

Procedures	Total	LAR	VLAR	p value
Laparoscopic operation (yes/no)	23/124	15/66	8/58	0.3635*
Conversion (yes/no)	9/14	6/9	3/5	1.0000*
Classic operations (yes/no)	124/23	66/15	58/8	0.3635*

* χ^2 test

Table 8. Intraoperative management (metastases and protective colostomy/ileostomy)

Procedures	Total	LAR	VLAR	p value
Liver metastasectomy (yes/no)	5/7	4/4	1/3	0.5758*
Protective colostomy (yes/no)	22/125	12/69	10/56	1.0000*
Protective ileostomy (yes/no)	13/134	8/73	5/61	0.7730*

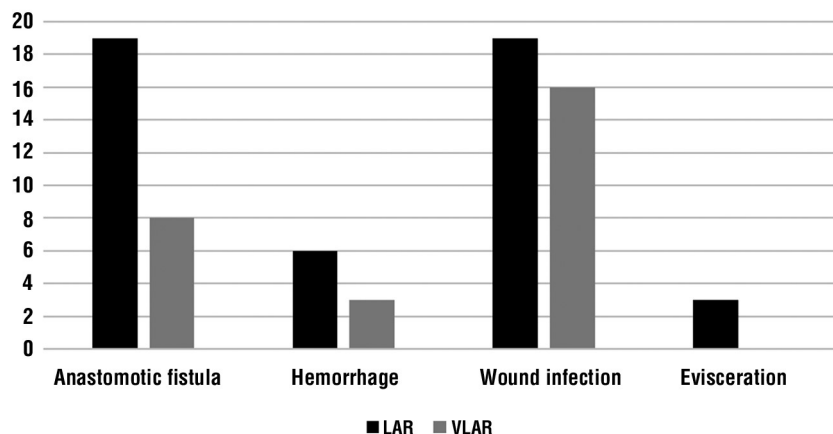
* Fisher's exact test

Table 9. Postoperative complications

Procedures	Total	LAR	VLAR	p value
Anastomotic fistula (yes/no)	27/120	19/62	8/58	0.1934*
Hemorrhage/Hematoma (yes/no)	9/138	6/75	3/63	0.5155*
Wound Infection (yes/no)	35/112	19/62	16/50	1.0000*
Evisceration (yes/no)	2/145	2/79	0/66	-

* Fisher's exact test

Graph 2. Postoperative complications LAR/VLAR



majority of patients who developed a fistula were over 60 years of age. The preoperative neoadjuvant treatment mostly associated with postoperative fistula was radiotherapy, in 13 cases (Table 10, Graph 3).

Comorbidities and biological parameters studied for their association with fistula occurrence were hypertension with ischemic cardiomyopathy, type II diabetes, low albumin level (< 3.5 g/dl) and anemia, as measured by hemo-

globin (< 13.5 g/dl males; < 12.0 g/dl females) and hematocrit (< 39% males; < 36% females) levels. The only parameter that presented statistically significance was diabetes type II association with fistulas in the VLAR group (Table 10).

Discussions

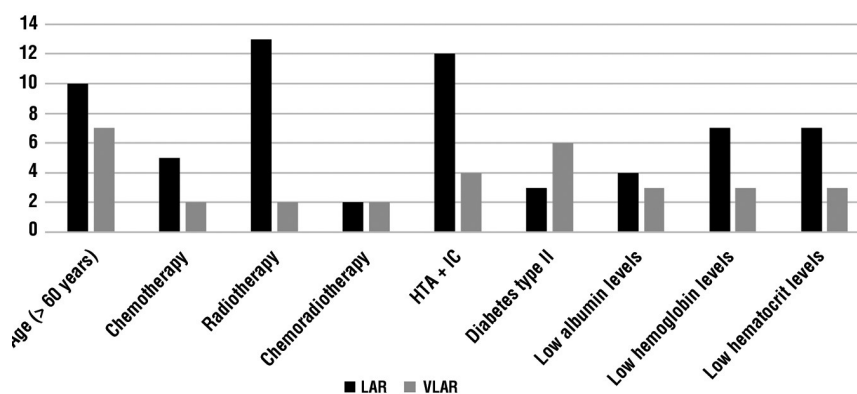
Oncological radical resection must be the first

Table 10. Comorbidities, biological parameters and preoperative treatment - fistula association

Fistula + Comorbidities	LAR	VLAR	p value
Age (>60years) (yes/no)	10/9	7/1	0.1895*
Chemotherapy (yes/no)	5/14	2/6	1.0000*
Radiotherapy (yes/no)	13/6	2/6	0.0870*
Chemoradiotherapy (yes/no)	2/17	2/6	0.5583*
**HTA + IC (yes/no)	12/7	4/4	0.6754*
Diabetes type II (yes/no)	3/16	6/2	0.0061*
Low Albumin levels (yes/no)	4/15	3/5	0.6334*
Low Hemoglobin levels (yes/no)	7/12	3/5	1.0000*
Low Hematocrit levels (yes/no)	7/12	3/5	1.0000*

* Fisher's exact test; ** HTA - hypertension, IC- ischemic cardiomyopathy

Graph 3. Comorbidities, biological parameters and preoperative treatment - fistula association



goal in rectal surgery for cancer. Preserving the sphincter function represents the second most important objective, aiming to improve the patients' quality of life (11,12).

If superior rectal tumors are technically easier to approach, the treatment for low rectal cancers represents a real challenge for all surgeons (5).

We considered by low rectal cancer those tumors located between 5-10 cm from the anal verge and very low those situated less than 5 cm from it (13). According to this, we excluded the cases of very low rectal cancers, for which an intersphincteric resection was made, these being the subject of other communicated studies (14-18).

Our study included two of the most used types of sphincter function saving procedures (SFSP) for low rectal cancer: low and ultralow anterior rectal resection. For low anterior rectal resections (LAR) was done a hand-sewn or a mechanic anastomosis, using a circular 29-31 EEA (end to end anastomosis) stapler (19). If local conditions were not allowing the low anterior rectal resection, we tried to go even lower and to do an ultralow anterior resection (VLAR) followed by a mechanical anastomosis (20).

Studies in the literature consider that the rate of complications after low or very low rectal resections, especially those related with local recurrence, is higher than after rectal amputation.

Our primary concern in choosing a sphincter-saving technique was oncological safety so a total mesorectal excision was performed and a 2 cm distal margin of resection was attempted in all patients (5,21). The postoperative pathological result confirmed the total mesorectal excision and that both distal and circular resection margins were free of tumor, in all cases.

The preoperative bowel preparation remains still a subject of debate. Most of the authors accept it has advantages (22) while studies are saying that it has no effect in lowering the rate of postoperative complications, in elective colorectal surgery (23). In our study, bowel preparation was done for all patients who did

not develop an occlusive syndrome.

By looking at the data collected, we can observe that the two studied groups present a homogenous distribution regarding the patients' age and gender and in what the tumor clinical and pathological features are presenting. Only tumor stenosis, as a local complication, was present in a significantly higher percentage in LAR and VLAR groups (40 from 54 cases), in which, it did not interfere with the possibility to perform an SFSP (24).

Preoperative radiotherapy was done in 65.98% of the cases. In 17.00% of cases, the association of chemotherapy was used to increase the tumor radiosensitivity (7,25). It is considered to be an important factor for better local control of the tumor, which increases the possibility of performing an SFSP (2,5,7). This may explain why the number of patients, in the study, who followed preoperative radiotherapy was significantly higher in the LAR group. No neoadjuvant treatment was done in cases in which a local complication, as occlusive stenosis or local hemorrhage, made necessary an emergency surgery or in which the patients specifically refused the oncological preoperative treatment.

For resectable liver metastases, complete resection can be done, along with the rectal tumor resection, in the same operative time or as a staged procedure (26). In our studied group, for the 12 patients with associated liver metastatic disease, in five of the cases a primary resection of liver metastasis was made. For the other seven cases, with non-resectable metastasis, a biopsy was performed, followed by a staged management (associating systemic and local chemotherapy with surgical resection, in case of conversion towards an operable stage) (26).

Reviews from the literature showed that the anastomotic time is shorter in a stapled than in a hand-sewn anastomosis (27). When comparing our two groups, we found that the operative time in the VLAR group was statistically significant longer (with an average of 165 ± 10.5 minutes). Our interpretation for these results is that anastomotic time repre-

sents only one individual variable influencing the overall operative time and that very low resections were technically more difficult to perform.

In selecting laparoscopic or open surgery, many variables should be considered as the tumor location and TNM stage, patient related factors and last but not least the experience of the surgical team (13). In the studied group, a laparoscopic approach was made only in 23 cases (15.64%) with a conversion rate of 39.13%. These results are due to the lack of technical materials necessary to perform, safely, the endoscopic procedure and to a learning curve that corresponded to the period studied. Also we have been confronted, very often, with an incorrect preoperative evaluation of the tumor location due to endoscopic evaluations that do not use a rigid endoscope (13).

We did not find any statistically significant differences between the analyzed surgical techniques in terms of associated postoperative morbidity or mortality, nor between the analyzed SFSP in terms of oncological and functional outcome (28).

When discussing postoperative local complications, the most severe seems to be the anastomotic fistula (29,30). The rate of postoperative anastomotic fistulas in patients with SFSP was 18.36% with no significant differences between LAR and VLAR groups. No statistically significant relation was found between the rate of postoperative anastomotic leakage and the risk factors studied (30) except for the type II diabetes who was statistically significant associated with fistula occurrence in the VLAR group.

The protective role of a temporary proximal diverting stoma can be considered as an option that might reduce the complications related to the anastomotic leakage (21,31). We did not practice this method systematically. We performed a protective ileostomy in 13 cases and a protective colostomy in 22 patients, all of them involving high-risk anastomosis.

Postoperative continence function was clinically evaluated from almost normal continence to mild incontinence not interfering with normal activity (32), for all patients. We

had no case of severe, invalidating incontinence, with the need for a permanent stoma.

The hospital stay was slightly longer for the patients who underwent SFSP, and among them for those with LAR, then in those with APR or HR, but with no statistical significance.

Conclusion

There was no statistical difference in terms of early postoperative outcomes among the sphincter function saving techniques analyzed in our study.

LAR and VLAR represent viable oncologic and functional alternatives to abdominoperineal resection, in the treatment of low rectal cancer.

A temporary proximal diverting stoma, in difficult anastomoses, can be considered as a procedure that might improve the management of fistula related complications.

The most important factor in achieving a good oncologic and functional outcome in low rectal cancer is choosing the adequate, tailored to the case surgical management.

Conflicts of Interest

Authors declare no conflict of interest.

Ethics of Approval

The study was conducted in accordance with the Declaration of Helsinki (1964) and had been approved by the Emergency County Hospital of Targu Mures Ethics Committee No. 3519/25.02.2015. All the patients were included in this study underwritten informed consent. They met all conditions of EU professional ethics, patients' identity being secret.

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