

Anterior resection of the rectum vs radical prostatectomy. Are there any differences in sexual rehabilitation?

Ressecção anterior do reto vs prostatectomia radical. Existem diferenças na reabilitação sexual?

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ABSTRACT

Purpose: The aim of this study was to evaluate the impact of penile rehabilitation in restoring erectile function in patients submitted to anterior resection of the rectum (ARR) or radical prostatectomy (RP), comparing the results between these two groups. **Materials and Methods:** We performed a unicenter retrospective cohort study, on patients evaluated in our multidisciplinary oncosexology consultation, between January 2015 and January 2018, submitted to RP or ARR (males) and presenting sexual dysfunction. We evaluate the patient and oncologic characteristics, the type of sexual dysfunction, marital status, assessed the International Index of Erectile Function (IIEF-5) on the first and last consultation and the therapeutic approach. A statistical analysis was performed. **Results:** A total of 55 patients were included, 60% (33) performed ARR and 40% (22) RP. Regarding the sexual dysfunction after surgery, erectile dysfunction (ED) was found in the majority of patients (>95%). On the initial IIEF-5 scoring, ARR and RP patients had, most frequently, severe or moderate ED (score 5-11), 78.8% and 59.1% respectively. When reassessed the IIEF-5 scoring of each patient during follow-up, there was an improvement in 69.7% of ARR patients and 72.7% of RP patients ($p=0.81$). Regarding the therapeutic approach, 84.8% of ARR patients used phosphodiesterase-5 inhibitors (PDE5i) exclusively, 3% used Alprostadil injection, while RP patients used 63.6% and 31.8%, respectively ($p<0.05$). **Conclusions:** Despite the technical differences of these surgeries, from the sexual point of view these patients benefit with a penile rehabilitation.

Keywords: Erectile Dysfunction. Prostate Cancer. Rectal Cancer.

INTRODUCTION

Prostate and colorectal cancer are the second and third, respectively, most commonly diagnosed cancer in men^{1,2}.

The surgical treatment of these cancers has improved over the past decades due to accurate pre-operative staging, appropriate referral for neoadjuvant therapy and development of new surgical technique, such as, total mesorectal excision (TME), essential to decrease the local recurrence and achieving better oncologic results in rectal cancer^{1,3}.

With improved oncological outcomes, functional results, as sexual function become increasingly important^{4,5}. Radical pelvic surgery is a common cause of sexual dysfunction, and every patient undergoing a surgical excision of rectal or prostate cancer will be at risk for these side effect.

It is expected that after these surgeries, 20-40% of patients will not resume sexual life and 23-69% of the men will identify onset sexual dysfunction⁶⁻⁸.

The term sexual dysfunction includes a wide spectrum of manifestations, including erectile dysfunction (ED), penile curvature, penile shortenings, dysorgasmia, ejaculatory disorders and climacturia⁹.

In rectal cancer, anterior resection of the rectum (ARR) has a lower risk of postoperative ED than abdominal perineal resection (APR), but can occur in 38% of the patients⁴. A permanent colostomy modifies the body image and increases the rate of sexual dysfunction⁹. Chemotherapy and radiotherapy may also affect sexual dysfunction^{1,5}.

Damage to the autonomic nervous system is the potential explanation for this dysfunction⁶. Injury to the sympathetic system, through the superior hypogastric plexus and hypogastric nerves

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results in ejaculatory dysfunction, whereas injury to the parasympathetic system, through the inferior hypogastric plexus, the pelvic and cavernous nerves results in urinary and erectile complications³. Even with the incorporation of nerve-preserving techniques in ARR or in the radical prostatectomy (RP), sexual dysfunction remains a recognisable complication in 10–35% and 14–38% of patients, respectively^{3,10,11}.

Recently, a vascular aetiology has been advocated, suggesting that loss of erections might lead to irreversible veno-occlusive disease, due to a continued cycle of smooth muscle cell death with damage to the cavernous tissue. Also patients with preserved neurovascular bundles might be at risk of venous leak, as a result of progressive fibrosis of the cavernosal tissue during the period of neurapraxia⁹.

Lately, investigators have searched for interventions that might improve sexual function after radical pelvic surgery. Various rehabilitation programs have been suggested and applied with different success rates^{12,13}. The rehabilitation program aims to shorten time to regain spontaneous erection, preventing penile corporal hypoxia and sequential cavernosal fibrosis, as explained before. To break this vicious cycle, the concept of early intervention was first described by Montorsi *et al.*¹⁴. The treatment options include: phosphodiesterase-5 inhibitors (PDE5I) scheduled or daily dosing; alprostadil preparations (injectables or urethral pellets) and vacuum constriction devices^{15,16}. These interventions have been used singly or in combination, after successful trials without catheterization following surgery¹⁶.

This novel idea of penile rehabilitation has gained interest worldwide, being extensively used in patients undergoing RP, with interesting results¹⁷. However, its success in patients undergoing ARR is unclear. This study aims to evaluate the impact of penile rehabilitation in restoring erectile function in patients who underwent ARR or RP, comparing the results between these two groups.

MATERIALS AND METHODS

We performed a unicenter retrospective cohort study, in an oncologic hospital, on male patients, who underwent RP for prostate cancer or ARR for rectal cancer and were referred to the multidisciplinary Oncosexology consultation due to sexual dysfunction, between January 2015 to January 2018. In ARR patients, a total or partial mesorectal excision was performed.

Inclusion criteria were male sex, surgical technique (RP or ARR) and having a sexually active life before the operation. Patients with benign lesions, whom failed to attend the follow up sessions and without a sexually active life were excluded from the study.

At the first evaluation, sexual dysfunction was characterized and an initial International Index of Erectile Function (IIEF-5) obtained. The IIEF-5 is a validated diagnostic tool for ED, composed of four questions about erectile function and one question regarding intercourse satisfaction. According to the IIEF-5, ED can be classified into five severity levels, ranging from none (22-25), to mild (17-21), mild-to-moderate (12-16), moderate (8-11), and severe (5-7)⁴.

After this evaluation, penile rehabilitation was prescribed, usually starting with PDE5I at least twice per week, but during follow-up it could be adjusted to Alprostadil injections. In some cases, these therapeutics were combined with the use of a vacuum erectile device (VED). This device uses negative pressure to distend the corporal sinusoids and to increase blood inflow to the penis. VED can be used with the aid of an external constricting ring which is placed at the base of the penis to prevent blood outflow, maintaining the erection for sexual intercourse¹⁸.

Patients were regularly assessed by a urologist, a nurse and, if needed, by a sex therapist and at every follow-up consultation, a new IIEF-5 was obtained (last registered).

We evaluated the patient and the oncologic characteristics, the type of sexual dysfunction, marital status, assessed IIEF-5 at the first and at every follow-up consultation as well as the therapeutic approach.

A descriptive analysis on the study population was performed. ED was defined as an IIEF-5 score lower than 22. A comparative analysis on ED was performed to evaluate the impact of penile rehabilitation, assessing the used therapeutic approach. A sub-analysis focused on comparing the results between the two groups of patients (RP VS ARR) was performed. Categorical data were compared using Pearson's chi-squared test and continuous variables with Student t-test. A two-sided p value <0.05 was considered as statistically significant. Statistical analysis was performed using SPSS®, version 23.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

We reviewed the data of patients who had undergone RP or ARR, and who were referred to our Oncosexology clinic to initiate penile rehabilitation, between January 2015 and January 2018. After excluding sexually inactive patients, deceased and those who failed to attend the follow up sessions, a total of 55 patients from the initial 67 were included, of whom 60% (n=33) underwent ARR and 40% (n=22) RP. The average age was 58.1 years (48-72) in the RP group and 61.9 (38-77) years in the ARR. The demographic and the clinical characteristics of the patients are shown in Table 1. The mean follow-up was 27.7 months (11–37 months). Regarding the marital status, the majority were married (87.9% in ARR vs 77.3% in RP) (p=0.7).

Table 1. Demographic and clinical characterization.

Characteristic	Radical prostatectomy (n=22, 40%)	Anterior resection of the rectum (n=33, 60%)	Total (n=55)	p
Age				0.25
31-45	-	6.1% (2)	3.6% (2)	
46-60	59.1% (13)	42.4% (14)	49.1% (27)	
61-74	40.9% (9)	42.4% (14)	41.8% (23)	
>75	-	9.1% (3)	5.5% (3)	
Marital status				0.7
Married	77.3% (17)	87.9% (29)	83.6% (46)	
Cohabitation	4.5% (1)	6.1% (2)	5.5% (3)	
Divorced	13.6% (3)	6.1% (2)	9.1% (5)	
Single	4.5% (1)	-	1.8% (1)	
Oncological treatment				<0.05
Surgery	72.8% (16)	3.0% (1)	30.9% (17)	
Surgery + QT	-	6.1% (2)	3.6% (2)	
Surgery + RT	27.2% (6)	-	11% (6)	
Surgery+QT+RT	-	90.9% (30)	54.5% (30)	

Age, Marital Status and Oncological treatment stratified in two groups: Radical Prostatectomy and Anterior Resection of the Rectum. Categorical data were compared using Pearson's chi-squared test and continuous variables with Student t-test. RT- radiotherapy, QT- chemotherapy.

Concerning the oncological treatment, for the ARR patients, a multimodal approach was common, with a neoadjuvant treatment being offered to 97% of patients (90.9% with radiotherapy plus chemotherapy and 6.1% with only chemotherapy). For the RP group, 27.2% did adjuvant radiotherapy. Concerning sexual dysfunction (table 2), ED was found in the majority of patients (97% in ARR vs 95.5% in RP). Regarding the initial IIEF-5 scoring, ARR patients had, more frequently, severe or moderate erectile dysfunction (score 5-11), than RP patients, 78.8% vs 59.1% ($p=0.95$). When evaluated the last registered IIEF-5 scoring, there was an improvement in 69.7% of ARR patients and 72.7% of RP patients ($p=0.81$).

Interestingly, married patients (in both groups) had a higher improvement in the IIEF-5 score than other patients ($p=0.046$). When we performed a comparison between the last registered IIEF-5 in RP and ARR patients, after penile rehabilitation, we observed a similar improvement, with 40.9% and 42.5% of the patients, respectively, with mild or no ED ($p=0.72$) (figure 1).

Regarding the therapeutic approach, 84.8% of ARR patients used PDE5I exclusively, 12.2% used Alprostadil injection, while RP patients used 63.6% and 31.8%, respectively ($p<0.05$). In patients with hypoactive sexual desire, a conservative approach was used, which included sex therapy and counseling.

Table 2. Sexual features.

Characteristic	Radical prostatectomy (n=22, 40%)	Anterior resection of the rectum (n=33, 60%)	Total (n=55)	p
Sexual dysfunction				0.69
Erectile dysfunction	95.5% (21)	97% (32)	96.3% (53)	
Hypoactive sexual desire	4.5% (1)		3.7% (2)	
Initial IIEF-5				0.95
5-7 severe ED	36.4% (8)	42.4% (14)	40% (22)	
8-11: moderate ED	22.7% (5)	36.4% (12)	31% (17)	
12-16: mild to moderate ED	31.8% (7)	12.1% (4)	20% (11)	
17-21: mild ED	9.1% (2)	3% (1)	5.5% (3)	
22-25: no ED	-	6.1% (2)	3.5% (2)	
Last registered IIEF-5				0.81
5-7 severe ED	9.1% (2)	6.1% (2)	7.3% (4)	
8-11: moderate ED	13.8% (3)	9.1% (3)	11% (6)	
12-16: mild to moderate ED	36.4% (8)	42.4% (14)	40% (22)	
17-21: mild ED	27.3% (6)	27.3% (9)	27.3% (15)	
22-25: no ED	13.6% (3)	15.2% (5)	14.4% (8)	
Therapeutic approach				<0.05
IPDE-5	63.6% (14)	84.8% (28)	76.5% (42)	
Alprostadil injection	31.8% (7)	12.2% (4)	20% (11)	
Conservative approach	4.6% (1)	3% (1)	3.5% (2)	

Sexual dysfunction, IIEF-5 and therapeutic approach stratified in two groups: radical prostatectomy and anterior resection of the rectum. Categorical data were compared using Pearson's chi-squared test and continuous variables with Student t-test.

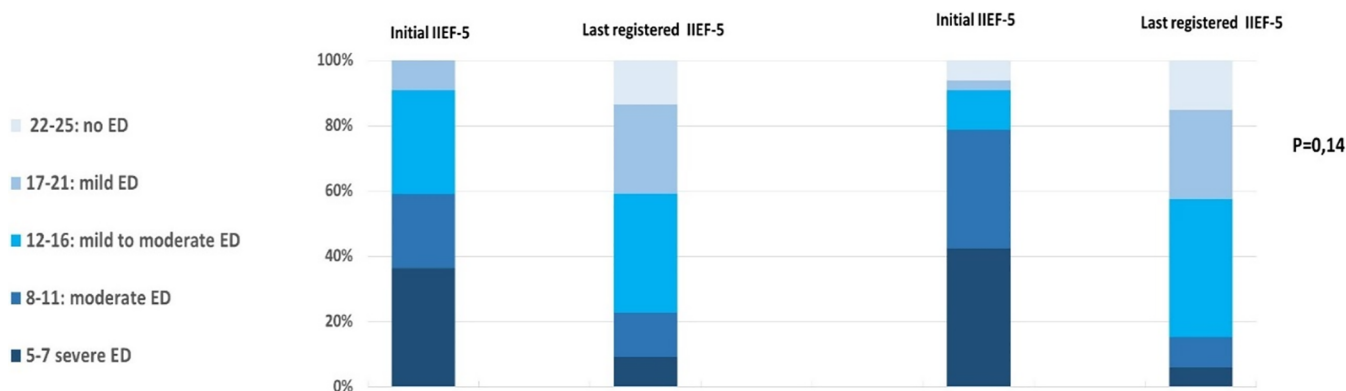


Figure 1. The impact of penile rehabilitation.

A comparative analysis on ED, assessing IIEF-5 before and after penile rehabilitation in radical prostatectomy and anterior resection of the rectum patients'. $P=0.14$.

DISCUSSION

Oncologic treatment outcomes usually consider mortality rates or disease-free survival. However, due to the success of these treatments, a shift from survival to improving quality of life is mandatory, considering sexuality a significant topic to be addressed. Amongst the dysfunctions that were found, ED represented the most common one. Although preoperative sexual dysfunction had not been evaluated, considering the average age of this group of patients, it was expected to find a low pre-surgical rate of ED. The cause of sexual dysfunction after a major pelvic operation is considered to be multifactorial. However, neuronal and vascular injury are the major risk factors to this impairment.

In this study, we observed that patients undergoing ARR had more frequently, severe or moderate erectile dysfunction at the initial IIEF-5 scoring, after surgery, compared to RP patients. Our results are similar to those from other authors. Wafi Attaallah, et al. found that 76% of the patients reported moderate-to-severe ED after surgical treatment of rectal cancer and Nassif et al. found 46% after RP^{19,20}. This difference is not fully understood, but it should be highlighted that these are two different surgical techniques and patients undergoing ARR more often also undergo radiotherapy and chemotherapy as neoadjuvant

therapeutics, with an unclear role of these therapies on sexual function. Despite these differences, after penile rehabilitation, we observed that both groups obtained a similar positive response, with improved IIEF-5 in almost 70% of the patients. This outcome was expected in RP group as Briganti et al. found that patients treated with IPDE5 had significantly higher 3-year erectile function recovery rate as compared with patients left untreated after RP (73 vs. 37%; $P < 0.001$)²¹. Interestingly, we found a similar benefit for ARR patients reinforcing the importance of penile rehabilitation in this group. Another remarkable finding in this study is the comparison of the used therapy for penile rehabilitation. When comparing the two groups, RP patients required more often Alprostadil Injection (31.8% vs 12.2%) to achieve similar results to the ARR group. Although there is no explanation for this difference, this may raise the question whether ARR patients are more responsive to IPDE5. Another interesting fact was a higher improvement in IIEF-5 found in married patients, probably acting as an incentive for intimacy and sexual recovery.

This study, however, has limitations. First, the small number of cases, similar to other published series, which limits the statistical power of the conclusions. Second, the study design, as a retrospective study it contains many bias, like selection bias (since only patients referred to the multidisciplinary

Oncosexology consultation were included). Therefore, we cannot generalize these conclusions to all patients that undergo these surgical approaches. Third, sexual function were not evaluated in the pre-operative period, not allowing us to evaluate the impact of these operations on sexuality. Ideally, a multicenter randomized prospective study with a larger sample would answer many questions raised in our study.

Doctors should inform patients about the risks and consequences of each procedure. The majority of patients never expose their sexual complains. Therefore, the clinician should evaluate this topic thoroughly. Urologists may be more familiarized to the sexual evaluation, as they treat sexual dysfunction, and general surgeons may be less sensitive to this issue. However, one of the major goals of this study was to compare the benefit of penile rehabilitation in these two groups of patients. As the benefit was identical, this indicates the importance of a proper and timely referral to an Andrology/Oncosexology consultation. The ideal therapeutic regimen for penile rehabilitation may vary, as it should be customized according to patients' expectations and degree of dysfunction, with therapeutic adjustment if necessary.

R E S U M O

Objetivo: O objetivo deste estudo foi avaliar o impacto da reabilitação peniana na recuperação da função erétil em pacientes submetidos a ressecção anterior do reto (RAR) ou a prostatectomia radical (PR), comparando os resultados entre esses dois grupos. **Materiais e Métodos:** Foi realizado estudo de coorte retrospectivo unicêntrico, em pacientes avaliados na nossa consulta multidisciplinar de oncosexologia, entre janeiro de 2015 e janeiro de 2018, submetidos a PR ou RAR (homens) com disfunção sexual. Avaliamos as características oncológicas dos pacientes, idade, estado civil, tipo de disfunção sexual, Índice Internacional de Função Erétil (IIEF-5) na primeira e última consulta e terapêutica utilizada. Foi realizada análise estatística. **Resultados:** Foram incluídos 55 pacientes, 60% (33) realizaram RAR e 40% (22) PR. Em relação à disfunção sexual após a cirurgia, a disfunção erétil (DE) foi encontrada na maioria dos pacientes (> 95%). Na pontuação inicial do IIEF-5, os pacientes com RAR e PR apresentaram, com maior frequência, DE moderada ou grave (escore 5-11), em 78,8% e 59,1% dos casos, respectivamente. Ao reavaliar a pontuação do IIEF-5 de cada paciente durante o acompanhamento, verificou-se melhoria em 69,7% dos pacientes com RAR e 72,7% dos pacientes com PR ($p = 0,81$). Quanto à abordagem terapêutica, 84,8% dos pacientes com RAR foram medicados com inibidores da fosfodiesterase-5 (PDE5I) exclusivamente e 3% com injeção de Alprostadil. Os pacientes com PR foram medicados com PDE5I em 63,6% e com injeção de Alprostadil em 31,8% ($p < 0,05$). **Conclusões:** Apesar das diferenças técnicas destas cirurgias, do ponto de vista sexual, os pacientes se beneficiaram com a reabilitação peniana.

Palavras-Chave: Disfunção Erétil. Câncer de Próstata. Câncer Retal.

CONCLUSIONS

Many cancer survivors report significant sexual dysfunction after treatment, although the prevalence rates vary according to the study design and treatment modality. Erectile dysfunction is the most frequent complication after radical pelvic surgery with a negative impact on the quality of life. However, rehabilitation programs have modified the natural history of postoperative erectile dysfunction. Patients should be informed about the risk of ED after radical pelvic surgery and about the potential benefits of an early penile rehabilitation. However, the most important aspect is the surgical procedure per se, which should be selected regarding the patient and tumour characteristics' preventing unnecessary neurologic damage.

In conclusion, this study demonstrates that ED is a common complication amongst patients undergoing ARR or RP. However, penile rehabilitation enables recovery for most patients, preventing the development of hypoxia-induced tissue damage, with obvious benefits and equal impact on both patient groups. Health care professionals and patients need to be aware of the potential advantages of penile rehabilitation for a timely start, with larger benefits.

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