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Review article

Surgical approach to the locoregional recurrence of cancer of the rectum

Aintzane Lizarazu, José M. Enríquez-Navascués,* Carlos Placer, Alberto Carrillo, Aitor Sainz-Lete, José L. Elósegui

Unidad de Cirugía Colorrectal. Servicio de Cirugía General y Digestiva, Hospital Donostia, San Sebastián, Spain

ABSTRACT

A literature review has been made on the pelvic recurrence of rectal cancer using the MedLine, Ovid, EMBASE, Cochrane and Cinahl data bases. Assessment of the locoregional recurrence must be made using imaging tests in order to rule out the presence of metastasis, as well as for locating its exact location within the pelvis. As the only curative treatment should be complete resection of the recurrence with negative margins, a pre-operative CT, NMR, endorectal ultrasound and PET-CT must be performed to determine its resectability. For a potential cure, radical resections must be made, with the technique varying according to whether the location is central (axial), posterior (presacral) or lateral, as well as treatment directed at the primary tumour. Neoadjuvant treatments, brachitherapy and intra-operative radiotherapy improve the local control results and survival in these patients.

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Abordaje quirúrgico de la recidiva locorregional del cáncer de recto

RESUMEN

Se ha realizado una revisión literaria relativa a la cirugía de la recurrencia pélvica del cáncer de recto utilizando las bases de datos MedLine, Ovid, EMBASE, Cochrane y Cinahl. La evaluación por pruebas de imagen de la recidiva locorregional debe realizarse tanto para descartar la presencia de metástasis como con el objetivo de localizar el sitio preciso (subsitio) de la misma dentro de la pelvis. Como el único tratamiento curativo será la resección completa de la recidiva con márgenes negativos, se deben realizar preoperatoriamente TC, RMN, ecografía endorrectal y PET-TC para determinar la resecabilidad. Para una potencial curación, se deben realizar resecciones radicales, variando la técnica según la localización de la recurrencia sea central (axial), posterior (presacra) o lateral, así como el tratamiento efectuado del tumor primario. Los tratamientos neoadyuvantes, la braquiterapia y la RTIO mejoran los resultados de control local y la supervivencia en estos pacientes.

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*Corresponding author.
E-mail address: josemaria.enriqueznavascues@osakidetza.net (J.M. Enríquez-Navascués).

Introduction

Locoregional recurrence (LRR) or isolated pelvic recurrence of rectal cancer after curative resection remains a serious and frustrating problem for patients and surgeons, where the only curative option is to perform rescue surgery or complete re-resection.[1] The two main reasons for this radical approach are, firstly, the disastrous symptomatic consequences of uncontrolled pelvic cancer (mainly pain and tenesmus), which is only partially and temporarily palliated by radiation therapy, and secondly, that many of these LR relapses remain situated exclusively in the pelvis, without dissemination.[2,3]

In recent years, the incidence of LRR has declined thanks to advances in the surgical treatment of rectal cancer and the use of neoadjuvant radio-chemotherapy (RCT), which provide better locoregional (LR) control of this disease. Moreover, a subtle change in the distribution of LRRs has been observed in relation to its location within the pelvis.[4-6] Overall, in the years prior to total mesorectal excision surgery, central pelvic recurrences were the most prevalent forms (peri-anastomotic and anterior). After combined adjuvant therapies, the lateral and posterior (presacral) forms are the most prevalent.[6]

Nevertheless, LRR rates remain between 2.6% and 32%,[2] depending on primary tumour and therapeutic factors (stage, margins, quality of the surgery, etc.). Some 70% of these recurrences occur in the first two years following surgery of the main tumour.

The average survival after diagnosis of recurrence without treatment is 6-7 months, with survival at five years being less than 5%[3] and with significant morbidity. With treatments such as radiotherapy (RT) combined or not with chemotherapy (CT), average survival increases to 10-17 months,[7] but tumour regression is rarely achieved and symptom relief occurs in only one third of patients. The only curative treatment is radical surgical resection, with better results if combined with a multimodal treatment with RCT.[1,4] For this reason, multidisciplinary teams should evaluate these cases. These teams must be made up of various specialists with experience in the evaluation and treatment of the disease. Despite this, LRR resection in rectal cancer does not have the same acceptance as resection of liver or lung metastases of colorectal origin due to the perception that the morbidity, mortality and associated sequelae of this type of surgery are excessive.

The aim of this study is to review the literature on diagnosis, management and surgical treatment with curative intent for LRR of rectal cancer.

Methods

A review was performed of the literature between 1999 to November 2010 on the surgical treatment of rectal cancer recurrence. A search was performed on the CINAHL, MedLine, Ovid, EMBASE and Cochrane databases, using the following key words: "rectal carcinoma", "recurrent rectal cancer", "local recurrence" and "surgery".

Classifications

There are various classifications for LRR in these types of tumours, but there is no universal consensus with regard to the recurrence. One is that described by the *Clínica Mayo* (Mayo clinic), which classifies according to the patients' symptoms (S0: asymptomatic, S1: symptomatic without pain, S2: symptomatic with pain) and the number of sites of fixation to the pelvic wall (F0: not fixed to the pelvic wall, F1: fixed at one site, F2: fixed at two sites, F3: fixed at three or more sites) (Figure 1). This publication has demonstrated a significant decrease in patient survival for those who presented pain and those with a tumour fixed to more than one site.[8]
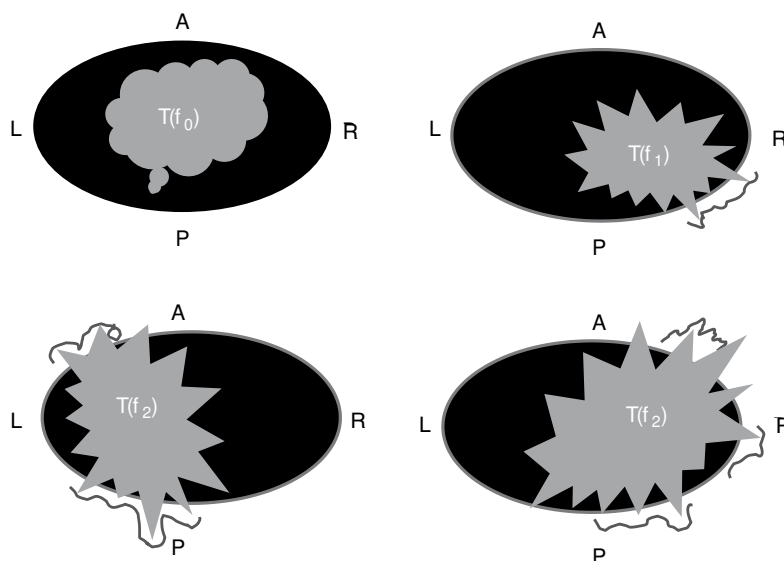
Figure 1 – Classification of pelvic recurrence according to the Clínica Mayo 1996.[4] f_0 indicates not fixed; f_1, fixed at one site (red line), f_2, fixed at 2 sites, f_3, fixed at 3 sites.
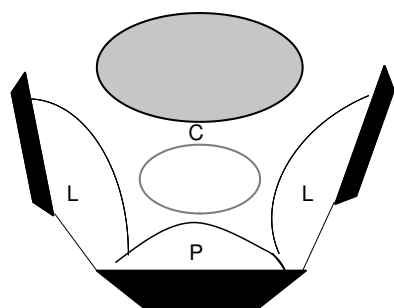
Figure 2 – Subsites of pelvic recurrence according to the Leeds group.[10] C indicates central; L, lateral; P, posterior.

The Memorial Sloan Kettering classification combines the location of recurrence in the pelvis with prior surgery performed: local (after transanal resection), axial anastomotic (after anterior resection), perineal-axial (after abdominoperineal resection), posterior (with sacrum or coccyx infiltration), anterior (with invasion of urogenital or gynaecological organs) and lateral (with infiltration of pelvic wall structures). Using this system, Moore et al[9] observed a significant reduction in complete resection (R0) in lateral tumours.

The Leeds group[10] proposed a pragmatic classification based on the anatomical location of the recurring lesion: *central* (confined to pelvic organs), *lateral* (lymphovascular and osteoligamentous structures of the lateral pelvic walls), *presacral* (in contact with or affecting the sacrum) and *composite* (sacrum and lateral walls) (Figure 2).

Presentation mode

One third of patients are asymptomatic and LRRs are diagnosed in routine postoperative follow-ups.[8,11] Anastomotic relapses may present as rectal bleeding and changes in bowel habits. Pain is the most significant symptom and is correlated with a lower rate of R0 resection and portends a worse prognosis.[11] Local recurrence after abdominoperineal amputation may present as lack of healing of the perineal wound, perineal mass, pelvic pain and intestinal obstruction due to entrapment of small intestine loops in the pelvic mass.[1] In general, 50% of all LRRs present with synchronous metastases. However, this figure may be higher (70%-75%) in series that exclusively analyse pelvic recurrence after neoadjuvant therapy.[6]

Preoperative evaluation

In addition to considering the general status and physiological reserve of patients, the preoperative evaluation should focus on the anatomical diagnosis and classification of the LRR, ruling out distant metastases. The presence of distant metastases would rule out the possibility of a curative surgical resection, although some authors have achieved acceptable results in patients with LRRs and one resectable lung or liver metastasis.[12,13] Given the high morbidity of resection, it should only be considered in very select cases.

A complete preoperative biochemical study needs to be carried out with special emphasis on the assessment of renal function, since altered creatinine may be an indication of renal failure. This is often associated with hydronephrosis and ureteral infiltration, which is typical of unresectable lateral recurrences. This is unlike advanced rectal tumours or primary rectosigmoid junction tumours that infiltrate ureters and that do not prevent their resection.[4,10] Although a high preoperative carcinoembryonic antigen (CEA) level may portend a worse prognosis, it does not provide information on the resectability of the recurrence.[1]

Whenever possible, a rectoscopy should be performed to evaluate the location and fixation of the tumour. It is also advisable to perform a complete colonoscopy to rule out colonic tumours synchronous with the LRR and obtain biopsies to confirm the diagnosis of intraluminal recurrences.

Radiological imaging tests should be performed to determine the stage of the LRR and identify the systemic recurrences. Endorectal ultrasound may differentiate fibrosis and recurrence, but it is limited by the disintegration of tissues after surgery and radiation therapy.[14,15]

One of the most useful tests is the thoracic-abdominopelvic CT, which has a sensitivity of 70% and a specificity of 85%, although it has difficulties in predicting infiltration of surrounding structures.[16-18] Although the CT cannot differentiate between fibrosis and tumours, it can accurately predict operability in 85% of cases.[16] The purpose of performing a thoracic-abdominopelvic CT is to help detect metastatic disease in the abdomen and chest.[16,17]

Although pelvic MRI and PET are not recommended for routine follow-up of patients after surgery for rectal cancer, it has been shown to be of great help when LRR is suspected.[17] Pelvic MRI is more accurate and is thought to be superior to CT in identifying pelvic organs, moreover, it has high sensitivity and specificity for detecting local invasions. The ability to differentiate soft tissues by means of different densities gives the CT a greater sensitivity and allows it to differentiate between normal, scar and tumour tissue. MRI is not as accurate for re-staging after neoadjuvant therapy due to the difficulty in evaluating previously irradiated tissues.[18] Furthermore, it has lower sensitivity for evaluation of the pelvic bone wall.[19,20]

As previously mentioned, PET is another test that may be useful, as it reveals the metabolic activity of any suspicious lesions. This helps confirm the presence of recurrence with greater accuracy than CT or MRI. PET-CT has greater sensitivity and specificity for identifying metastases and evaluating LRR when compared to PET.[19] The accuracy of PET in detecting LRR in the previously irradiated pelvis is 87%.[20] In some cases, PET-CT may help establish the diagnosis through the form, location and uptake of 18-fluorodeoxyglucose (FDG), and is especially valuable for lymph node recurrences. In some select cases where PET findings are indicative of recurrence, surgery may be considered even without confirmatory biopsy. PET-CT has its limitations, such as the proximity to the bladder, since physiological uptake of FDG by this organ changes the accuracy. PET-CT also has difficulties in detecting small recurrences and tumours with low metabolic activity, such as mucinous tumours.[17,20]

Whenever possible, histological confirmation of the recurrence should be obtained prior to surgery. Biopsies may

be performed by colonoscopy if the recurrence is intraluminal, or by CT-guided needle if colonoscopy cannot be performed. The interpretation of these samples may be difficult as they often come from previously irradiated patients. In the absence of malignant histology, surgical exploration should be considered, with possible resection in patients with PET-CTs indicating suspected malignancy, and in lesions that have increased in size during follow-up.[1]

Resectability

Resectability is defined as the possibility of complete surgical resection with negative microscopic margins (R0) with acceptable postoperative morbidity and mortality. Since resection is the only curative treatment, patients in whom an R0 resection can be performed, as well as those in whom it is contraindicated, should be identified in the preoperative period. This may be difficult or impossible in some patients undergoing resection with curative intent, as resectability will have to be determined in the operating room. Survival with affected microscopic and macroscopic margins after resection will be significantly lower, and therefore these resections are often palliative.[4,10,13]

Rescue surgery is considered contraindicated in patients with LRR of rectal cancer, extrapelvic unresectable disease and the presence of positive para-aortic lymph nodes. However, some authors have achieved acceptable results in patients with local recurrence and localised and potentially resectable liver and lung metastases.[12,21]

Multivariate analysis has indicated that the factors that decrease the likelihood of achieving a surgical resection with negative margins are male gender, advanced age at diagnosis of primary tumour, abdominoperineal amputation as primary surgery, advanced stage of primary tumour, high carcinoembryonic antigen levels and the presence of pain as a symptom.[9,13]

As for recurring disease, the location of the tumour recurrence in a particular area of the pelvis and the degree of local invasion are the two most important factors in determining resectability.[6,8,9] Axial or anterior recurrence is associated with a greater rate of complete resection.[6] When recurrence is located laterally, the likelihood of achieving an R0 resection decreases, therefore, the presence of a ureteral invasion with hydronephrosis and entrapment of iliac vessels by the tumour is considered a contraindication to surgery.[10] Oedema of lower extremities and perineal pain or pain at the root of the thigh are ominous signs of lateral and obturator tumour growth.

Another contraindication to surgery is invasion of the sacral promontory or the tumour growing over the piriformis muscle and through the sciatic notch (usually manifested by pain/discomfort in the buttocks). Although sacral infiltration in levels S1and S2 is considered a relative contraindication, nerve root infiltration in S1 and S2 is an absolute contraindication due to the high morbidity associated with resection.[4,13,22] In all cases one should take into consideration that patient comorbidities may preclude surgery regardless of the resectability of the local recurrence.

Neoadjuvant therapy

As mentioned earlier, the only curative treatment is complete surgical resection. However, this may prove difficult due to the need for extensive resection and by the distortion of anatomical planes by previous surgery. RCT reduces LRR after surgery of primary cancer and is often used prior to recurrence surgery in those treatment-naïve patients with pelvic recurrence, i.e. those who did not receive adjuvant therapy for the original tumour. By using RCT, there has been a 37% to 69% increase in local control of the disease and a 61% reduction in relative risk of LRR.[23,24] As with the treatment of advanced original rectal tumours, recurrent tumours should be re-staged after completion of RCT as it is common to detect disseminated disease in the rest period after RCT.[1,2,3,7,13]

For patients with recurrence and previous radiation, the dosage and field of radiation must be considered, which limit the possibilities for re-radiation. In the past, radiation therapy was not used on patients with previous radiation for fear of side effects. However, in recent years, preoperative RCT has been found to be safe and effective for local recurrence of rectal cancer when used at doses of 30Gy in selected patients, with low acute toxicity and acceptable late complications. Large multicentre studies are required to determine a safe interval between initial radiation therapy and re-radiation.[25,26]

Moreover, brachytherapy, administered with intraluminal devices or inserting needles or seeds, enables the administration of high doses of radiation concentrated in specific areas, minimising injuries to normal tissues. This has been used with great effect in the management of LRR of rectal cancer.[27,28]

Those centres that have intraoperative radiation therapy (IORT) use this therapeutic modality for such cases, achieving greater locoregional control of the disease, R0 resections and survival.[29,30] The need for incorporating IORT (or brachytherapy) into multimodal treatment with external radiation therapy, chemotherapy and surgery is increasingly being accepted.[28,30] Re-recurrence after IORT often occurs when negative macroscopic surgical margins are not achieved. Interestingly, despite the high doses of radiation administered, the rates of treatment failure with IORT indicate that recurrence usually occur in the presacral area, an area that falls within the radiation field. This leads one to assume that the origin of these recurrences may be related to tumour cells trapped in the lateral pelvic lymph nodes.[5,6]

Surgical approach

The main goal of surgery is to achieve a R0, which requires extensive resection, with en bloc extirpation of adjacent organs. Resection is defined as extended radical resection when performing exeresis of surrounding organs.[11] Another goal of surgery is to preserve unaffected adjacent organs, which will, as much as possible, maintain the patient's quality of life. If resection is not possible, surgical palliation should be considered.

Depending on the case, surgery will require the collaboration of various doctors, including plastic surgery, urology, trauma, and neurosurgery specialists. In all cases, ureteral guides must be inserted prior to surgery to help identify ureters during surgery. Median laparotomy is to be performed in the Lloyd-Davies position. Distant disease and peritoneal disease must be ruled out and resectability must be evaluated since half of all patients with local recurrence will have disseminated disease or unresectable tumours. Dissection of the pelvis will begin some distance from the site of fixation, taking into account that the specific surgical procedure will vary based on the extent of the tumour.[10,13,21]

Resection for *axial recurrences* will depend on the primary surgery. If a patient underwent an anterior resection, then the tendency will be towards an abdominoperineal amputation. However, in very select cases with high recurrence, one may opt for sphincter-sparing surgery, with the difficulty that is involved in achieving a complete resection due to the change in surgical plans caused by prior surgery and radiation therapy. The dissection plane must be performed externally to the plane of the previous surgery.[8,20]

The presence of an anterior recurrence implies an invasion of the uterus, vagina, bladder, prostate and seminal vesicles. A posterior and lateral dissection should be attempted before evaluating the anterior fixation of the tumour. The extent of resection will depend on the affected organs, which must be resected en bloc. If there is an invasion of the uterus and vagina, the surgeon must perform a posterior exenteration with residual rectal resection, hysterectomy and vaginectomy (total or partial). Reconstruction with myocutaneous flaps may be performed if primary closure is not desirable.[31-34] If the prostate has been infiltrated, the surgeon may opt for an en bloc prostatectomy. If there is an invasion of the bladder dome, the surgeon may perform a wedge-resection of the bladder or a partial cystectomy with primary closure. However, if there is an invasion of the bladder trigone, a total pelvic exenteration should be performed with resection of all pelvic organs. Many surgical techniques have been described for intestinal and urologic reconstruction, with the formation of a Bricker ileal conduit[10] or a double barrelled wet colostomy[35] being the most frequently used.

Lateral invasion of the tumour is a limiting factor for attempted curative resection, as it is associated with a worse prognosis and a lower chance of achieving an R0 resection. Iliac vessels and proximal ureters must be identified with the help of ureteral guides prior to pelvic dissection. While infiltration of soft tissues surrounding the piriformis muscle may be resected with adequate reconstruction, it is very unlikely that an R0 resection can be achieved in bone wall invasions. However, if complete resection is doubtful, IORT may be administered for treatment of the lateral resection margin, keeping in mind that intraoperative biopsies can be obtained. It has been observed that lateral recurrences are often less resectable than central and anterior recurrences.[1,4,5,9,10]

When the recurrence is *posterior*, the presacral fascia can be resected en bloc with an elevation of the periosteum, but a bone invasion requires resection of the sacrum. In these cases, a sacrectomy should be performed with en bloc resection of the neorectum. In order to perform a resection of the sacrum, the patient must be placed in the prone position.[10] Sacrectomy is feasible below S2, but is associated with significant blood loss. To significantly reduce haemorrhaging during the sacrectomy, the surgeon may opt for ligation of the internal iliac vessels, with prior ligation of the internal iliac artery and the dorsal venous complex of the penis before tying the iliac vein.[3,22] The S2 nerve roots should be identified and dissected in order to prevent complications from their injury. Prior to the sacrectomy, the sacrospinous and sacrotuberous ligaments must be sectioned.[22] These interventions must be performed by specialised teams.

After abdominoperineal amputation, the perineal defect may be substantial, especially after a sacrectomy. Various techniques have been used for reconstruction, ranging from primary closure to myocutaneous flaps. Primary closure may be performed on a omentoplasty or an absorbable or biological mesh, but the best results in terms of healing and surgical wound infection have been achieved using pedicled myocutaneous flaps.[3,8,31-34] Gracilis muscle, which provides small amounts of tissue, may be used for these flaps, as well as gluteal muscles, and rectus abdominis muscle, which provides the best results.[32]

Conclusions

LRR of rectal cancer remains a major therapeutic challenge. Although surgery is the only curative treatment, multimodal treatment and the assessment of these patients by a multidisciplinary team are important. A complete preoperative evaluation is important to identify morbidity and sequelae of this surgery, as well as resectability, although sometimes this can only be confirmed intraoperatively. The surgical technique indicated for recurrence will depend not only on the modality of treatment of the primary disease, but also on the precise intrapelvic anatomical location of the recurrence, with the goal of surgery being to achieve an R0. In these patients, treatments with preoperative RCT, brachytherapy and IORT allows for improved LR control of the disease and survival. With this radical approach, 33% of patients survive 3-5 years, 33% will present a new LRR and another third will develop disseminated disease.[1,3,30]

Conflict of interest

The authors affirm that they have no conflict of interest.

R E F E R E N C E S

1. Bouchard P, Efron J. Management of recurrent rectal cancer. Ann Surg Oncol. 2010;17:1343-56.
2. Abulafi AM, Williams NS. Local recurrence of colorectal cancer: the problem, mechanisms, management and adjuvant therapy. Br J Surg. 1995;81:7-19.
3. Sagar PM, Pemberton JH. Surgical management of locally recurrent rectal cancer. Br J Surg. 1996;83:293-304.
4. Ferenschid FTJ, Vermaas M, Verhof C, Dwarkasing RS, Eggermont AMM, De Wilt JHW. Abdominosacral resection

for locally advanced and recurrent rectal cancer. Br J Surg. 2009;96:1341-7.

5. Kusters M, Wallner C, Lange MM, DeRuiter MC, Van de Velde CJH, Moriya Y, et al. Origin of presacral local recurrence after rectal cancer treatment. Br J Surg. 2010;97:1582-7.

6. Kusters M, Marijnen CA, Van de Velde LJ, Rutten HJ, Lahaye MJ, Kim JH, et al. Patterns of local recurrence in rectal cancer;a study of the Dutch TME trial. Eur J Surg Oncol. 2010;36:470-6.

7. Palmer G, Martling A, Cedermark B, Holm T. A population-based study on the management and outcome in patients with locally recurrent rectal cancer. Ann Surg Oncol. 2007;14:447-54.

8. Hahnloser D, Nelson H, Gunderson LL, Hassan I, Haddock MG, O'Connell MJ. Curative potential of multimodality therapy for locally recurrent rectal cancer. Ann Surg. 2003;237:502-8.

9. Moore HG, Shoup M, Riedel E, Minsky BD, Alektiar KM, Ercolani M, et al. Colorectal cancer pelvic recurrences: determinants of resecability. Dis Colon Rectum. 2004;47:1599-606.

10. Mirnezami AH, Sagar PM, Kavanagh D, Witherspoon D, Lee P, Winter P. Clinical algorithms for the surgical management of locally recurrent rectal cancer. Dis Colon Rectum. 2010;53:1248-57.

11. Heriot AG, Byrne CM, Lee P, Forbes H, Thompson MR, Stamatakis JD, et al. Extended radical resection: the choice for locally recurrent rectal cancer. Dis Colon Rectum. 2008;51:284-91.

12. Hartley J, Lopez R, Paty PB, Wong WD, Cohen AM, Guillem J. Resection of locally recurrent colorectal cancer in the presence of distant metastases: can it be justified? Ann Surg Oncol. 2003;10:227-33.

13. García-Aguilar J, Cromwell JW, Marra C, Lee SH, Madoff RD, Rothenberger DA. Treatment of locally recurrent rectal cancer. Dis Colon Rectum. 2001;44:1743-8.

14. Rontondano G, Esposito P, Pellecchia L, Novi A, Romano G. Early detection of locally recurrent rectal cancer by endosonography. Br J Radiol. 1997;70:567-71.

15. Siddiqui A, Fayiga Y, Huerta S. The role of endoscopic ultrasound in the evaluation of rectal cancer. Int Semin Surg Oncol. 2006;3:36-46.

16. Beets-Tan RG, Beets GL, Borstlap AC, Oei TK, Teune TM, Von Meyenfeldt MF, et al. Preoperative assessment of local tumor extent in advanced rectal cancer: CT or high-resolution MRI? Abdom Imaging. 2000;25:533-41.

17. Schaefer O, Langer M. Detection of recurrent rectal cancer with CT, MRI and PET/CT. Eur Radiol. 2007;17:2044-54.

18. Messiou C, Chalmers A, Boyle K, Wilson D, Sagar P. Preoperative MR assessment of recurrent rectal cancer. Br J Radiol. 2008;966:468-73.

19. Votrubova J, Belohlavek O, Jaruskova M. The role of FDG-PET/CT in the detection of recurrent rectal cancer. Eur J Nucl Med Mol Imaging. 2006;33:779-84.

20. Moore H, Akhurst T, Larson LM, Minsky BD, Mazumdar M, Guillem JG. A case-controlled study of 18-fluorodeoxyglucose in the detection of pelvic recurrence in previously irradiated rectal cancer patients. J Am Coll Surg. 2003;197:22-8.

21. Schurr P, Lentz E, Block S, Kaifi J, Kleinhans H, Cataldegirmen G, et al. Radical redo surgery for local rectal cancer

recurrence improves overall survival: a single center experience. J Gastrointest Surg. 2008;12:1232-8.

22. Moriya Y, Akasu T, Fujita S, et al. Total pelvic exenteration with distal sacrectomy for fixed recurrent rectal cancer in the pelvis. Dis Colon Rectum. 2004;47:2047-50.

23. Dresen RC, Gosens MJ, Martijn H, Nieuwenhuijzen GA, Creemers GJ. Radical resection after IORT-containing multimodality treatment is the most important determinant for outcome in patients treated for locally recurrent rectal cancer. Ann Surg Oncol. 2008;15:1937-47.

24. Sebag-Montefiore D, Stephens RJ, Steele R, Monson J, Grieve R, Khanna S, et al. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. Lancet. 2009;373:811-20.

25. Valentini V, Morganti AG, Gambacorta MA, Mohiuddin M, Doglietto GB, Coco C, et al. Preoperative hyperfractionated chemoradiation for locally recurrent rectal cancer in patients previously irradiated to the pelvis: a multicentric phase II study. Int J Radiat Oncol Biol Phys. 2006;64: 1129-39.

26. Mohiuddin M, Marks G, Marks J. Long-term results of reirradiation for patients with recurrent rectal carcinoma. Cancer. 2002;95:1144-50.

27. Kuehne J, Kleisli T, Biernacki P, Girvigian M, Streeter O, Corman ML, et al. Use of high dose-rate brachitherapy in the management of locally recurrent rectal cancer. Dis Colon Rectum. 2003;46:895-9.

28. Sun Myint A, Mukhopadhyay T, Ramani VS, Perkins K, Snee AJ, Jelley F, et al. Can increasing the dose of radiation by HDR brachitherapy boost following preoperative chemoradiotherapy for advanced rectal cancer improve surgical outcomes? Colorectal Dis. 2010;12(suppl 2):30-6.

29. Willet CG, Czito BG, Tyler DS. Intraoperative radiation therapy. Clin J Oncol. 2007;25:971-7.

30. Vermaas M, Nuyttens JJ, Ferenschild FT, Cornelis Verhoef C, Eggermont AMM, De Wilt JHWAT Reirradiation, surgery and IORT for recurrent rectal cancer in previously irradiated patients. Radiother Oncol. 2008;87:357-60.

31. Moreno-Sanz C, Manzanera-Díaz M, Clerveus M, Cortina-Oliva FJ, De Pedro-Conal J, Picazo-Yeste J. Reconstrucción pélvica tras amputación abdominoperineal del recto. Cir Esp. 2010.

32. Casal Núñez JE, Cáceres Alvarado N, De Sanildefonso Pereira A, Toscano Novelle MB, García Martínez MA, Jove Albores P. Resección abdominoperineal en cáncer anal: reconstrucción del periné con colgajo miocutáneo de músculo recto anterior abdominal. Cir Esp. 2010.

33. Radice E, Nelson H, Mercill S. Primary myocutaneous flap closure following resection of locally advanced pelvic malignancies. Br J Surg. 1999;86:349-54.

34. Shibata D, Hyland W, Busse P, Kim HK, Sentovich ST, Steele G. Immediate reconstruction of the perineal wound with gracilis muscle flaps following abdominoperineal resection and intraoperative radiation therapy for recurrent carcinoma of the rectum. Ann Surg Oncol. 1999;6:33-7.

35. Golda T, Biondo S, Kreisler E, Frago R, Fraccalvieri D, Millan M. Follow-up of double-barreled wet colostomy after pelvic exenteration at a single institution. Dis Colon Rectum.