Historically, locally advanced rectal cancers with invasion of tumor into adjacent organs (T4 N1,2 tumors) have been considered poor prognosis cancers treated with palliative intent. However with the advent of multi-modality therapy and improvement in surgical reconstructive techniques, extended resections for rectal tumors are possible with acceptable patient morbidity and excellent oncological outcomes.

Key words: locally advanced rectal cancer, resection

INTRODUCTION

Colorectal cancer is the 4th most prevalent cancer in the US with 39,670 new case of rectal cancer estimated to be diagnosed in 2010. Of the 51,000 anticipated colorectal cancer deaths in 2010, at least one third of those will be due to rectal cancer and 10% of diagnosed rectal cancers will be from locally advanced or T4 disease.¹ Historically T4 or rectal cancers locally invading into adjacent organs was considered inoperable disease. Unfortunately this led to the terminal symptoms of rectal cancer such as multiple fistulas, defecation difficulties and intractable pain due to the involvement of pelvic nerves, which are extremely debilitating and can be particularly challenging to palliate. Significant improvements in the treatment of rectal cancer have occurred in the last 20 years to reduce the incidence of local recurrence of rectal cancer following surgery, the most significant being development of effective neo-adjuvant chemo-radiotherapy and the widespread use of Total Mesorectal Excision (TME) of the rectum during rectal cancer surgery.²,³ The concept of extensive resection of multiple pelvic organs to resect pelvis tumors was first described by Dr Brunschwig, a gynecologist working at Memorial Hospital in New York in the 1940’s. While the morbidity and mortality rates he reported were extremely high subsequent improvements in reconstructive techniques and peri-operative management have made extended resections and exenterations for pelvic malignancies a much more palatable treatment option.

In this paper we shall review the perioperative treatment, surgical technique, and clinical outcomes of patients with locally advanced rectal cancer.

INCIDENCE

Approximately 40,000 patients are diagnosed each year with rectal cancer in the USA and of those approximately 25% will succumb to their disease. Ten percent of those patients with rectal cancer will present with locally advanced or T4 disease in the absence of distant metastatic
With appropriate multimodality treatment the mortality rates at 5 years can be as low as 40%. With the advent of effective neo-adjuvant chemotherapy and radiotherapy up to 60% of locally advanced and specifically 55% of T4 tumors can be downstaged. This may enable a TME resection to be performed. Even if downstaging to T3 disease is not possible, tumor shrinkage in response to the neoadjuvant treatment may help to facilitate preservation of adjacent organs at surgery.

**IMAGING/STAGING**

Pre-operative imaging is essential to identify the extent to which the tumor invades into adjacent organs. As mentioned before the most important factor to reduce the incidence of local recurrence is obtaining an R0 resection with no residual microscopic disease left. Tumor invasion into the high sacrum (involvement of S2), encasement of the sciatic nerve or common ileac vessels, extensive retroperitoneal metastatic lymph nodes and unresectable distant metastatic disease all make it impossible to obtain an R0 resection. These patients are therefore considered inoperable.

High quality pre-operative imaging is essential for appropriate patient selection. It also gives the surgeon an idea of the extent of resection necessary and which organs needed to be resected, i.e. need for sacrectomy or prostatectomy. High resolution pelvic MRI with or without gadolinium contrast is currently the best radiological test for determining local tumor spread in the pelvis, however endo-anal ultrasound is also a useful adjunct. Although the overall accuracy of MRI to detect tumor adjacent organ spread and lymph node involvement is reduced in the irradiated pelvis from 92% to 66%, it still offers the best imaging for pre-operative planning of the appropriate surgical procedure.

This is because sensitivity and specificity of endo-anal ultrasound following neo-adjuvant treatment is inferior to that of MRI, 77.8% and 37.5% respectively compared to 75% and 88% with MRI. EUS however can still have a role in identifying pelvic lymphadenopathy. PET scanning may also be used to rule out or clarify suspected distant metastatic disease but has limited role in staging of pelvic disease either pre or post neo-adjuvant treatment.

**PREOPERATIVE CHEMORADIATION**

Neo-adjuvant radiotherapy has been standard of care for locally advanced rectal cancer (T3 and T4 tumors). Numerous studies have demonstrated a reduction in local recurrence of rectal cancer compared to surgery alone. A meta analysis published in 2000 by Camma et al of 14 randomized control trials comparing pre-op radiotherapy and surgery to surgery alone demonstrated an improved overall survival for RT and surgery with an odds ratio of 0.84 and a p-value of 0.04. Pre-operative RT can be given either as short course radiation with large fractions (5 x 5 Gy) for 1 week, followed by immediate surgery or as long course, 5 – 6 weeks of conventional fractionation (1.8 – 2.0 Gy) and surgery 4 – 6 weeks later. No trial has shown differences between the two approaches. However with the advent of adding chemotherapy to neo-adjuvant treatment long course treatment has become more popular.

### TABLE 1

**OUTCOMES FOLLOWING TOTAL PELVIC EXENTERATION FOR LOCALLY ADVANCED RECTAL CANCER**

<table>
<thead>
<tr>
<th></th>
<th>No of patients</th>
<th>Operative deaths</th>
<th>Local recurrence</th>
<th>5 year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hong Kong, 2000</td>
<td>15</td>
<td>0</td>
<td>ns</td>
<td>64%</td>
</tr>
<tr>
<td>Taivan, 2001</td>
<td>50</td>
<td>1</td>
<td>ns</td>
<td>49%</td>
</tr>
<tr>
<td>Yokohama, 2003</td>
<td>71</td>
<td>0</td>
<td>ns</td>
<td>54%</td>
</tr>
<tr>
<td>Netherlands, 2007</td>
<td>32</td>
<td>1</td>
<td>22%</td>
<td>52%</td>
</tr>
<tr>
<td>Tokyo, 2009</td>
<td>91</td>
<td>0</td>
<td>9%</td>
<td>52%</td>
</tr>
</tbody>
</table>

### TABLE 2

**OUTCOMES FOLLOWING SACRAL RESECTION FOR LOCALLY ADVANCED RECTAL CANCERS**

<table>
<thead>
<tr>
<th></th>
<th>No of pts</th>
<th>Operative deaths</th>
<th>Local recurrence</th>
<th>5 year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands, 2009</td>
<td>8</td>
<td>0</td>
<td>22%</td>
<td>56%</td>
</tr>
<tr>
<td>Poland, 2009</td>
<td>158</td>
<td>0</td>
<td>4.4%</td>
<td>68%</td>
</tr>
<tr>
<td>Japan, 2003</td>
<td>20</td>
<td>0</td>
<td>ns</td>
<td>47%</td>
</tr>
</tbody>
</table>
The rational for adding chemotherapy to a neo-adjuvant regime is compelling. Chemotherapy acts as a sensitising agent for radiotherapy, improving its efficacy. It allows for down staging of tumors to facilitate sphincter preserving surgery or in the case of T4 tumors, preservation of more organs at surgery and also allows for easier systemic treatment of micrometastatic disease. Complete remission rates of up to 30% have been demonstrated following neo-adjuvant chemotherapy compared to 10% with radiotherapy alone. Addition of infusional 5-FU to pre-op RT reduced rates of local recurrence and increases rates of both tumor regression and complete remission of the tumor. Recently capcitabine has also been substituted as a radiosensitising chemotherapeutic agent with similar results. Addition of post operative chemotherapy, particularly if a clinical response to pre-operative treatment has been seen is also advocated.

**TYPES OF OPERATION**

The type of the operation preformed depends on the distance of the tumor from the anal sphincters, and the extent of spread into the adjacent organs. The operation can be divided into 2 distinct phases, the first being the resection phase and the second being the reconstructive phase. The types of resections are categorized by the organs resected in continuity with the rectum.

The most common operations include total exenteration for large bulky rectal tumors invading bladder or prostate; posterior exenteration for women with tumors invading the uterus; anterior exenteration for sigmoid cancers invading posterior wall of bladder and anterior wall of uterus; extended resections for cancers focally invading pelvic structures (seminal vesicle, vagina, bladder, ureter, autonomic plexus) or metastatic to lymph nodes in pelvic side wall. Less commonly performed are sacral resections for tumors that invade or densely adhere to sacrum or coccyx: APR with sacrectomy or sacropelvic exenteration.

The reconstructive portion depends on the extent of the resection. The colon can be re-anastomosed to the rectum or the anal canal if the external sphincters are intact. When the bladder has been removed, urinary diversion is required, either by ileal conduit or by continent diversion. Dead space in the pelvis can lead to abscess formation and, when possible, should be filled with omentum. Large defects in the perineal skin or vagina may need to be filled with rectus or gracilis myocutaneous flaps.

**METHODS OF RESECTION**

Patients are given a bowel preparation the day before surgery and prophylactic antibiotics at induction of anesthesia. Depending on the type of resection the operation is either in one or two stages. Initially the patient is placed in the lithotomy position to allow access to the pelvis anteriorly and the perineum.

If sacral resection is planned a second stage is necessary and the patient is turned prone for the second part of the operation. Pre-operative ureteric stenting can help protect and identify ureters intraoperatively during mobilization and for APR’s, suturing of the anus also helps reduce fecal contamination. As a general rule adherence to adjacent structures must be assumed to be invasion of tumor into the adjacent viscus and all or part of needs to be resected with the tumor en bloc. Total exenteration A total pelvic exenteration is the removal of the rectum, bladder; with the vagina, uterus, cervix and parametrium in the female and prostate and seminal vesicles in the male.

The first step is to inspect the abdomen looking for disseminated peritoneal disease or small liver metastases not picked up on pre-op imaging which would change management. The origin of the inferior mesenteric artery at the aorta is then dissected. Retropertitoneal lymph nodes are inspected for metastatic disease, which might indicate unresectable disease if not easily removed. The ureters are identified and preserved. They are not transected until resectability is confirmed, thus also allow for monitoring of urine output. The inferior mesenteric artery are then ligated and transected. The recto-sigmoid colon is then transected approx 10cms proximal to the tumor.

The rectum is then dissected posteriorly down to the levator ani muscle. Care should be taken to avoid the pelvic nerves if possible. At this point the bladder is mobilized from the retro pubic space and the lateral bladder pillars attached to the lateral pubic rami are ligated and transected. If the patient is female the cardinal ligaments which support the vagina and cervix are transected and ligated at the pelvic sidewall. In a male patient the dissection is continued anteriorly to include the prostate gland. At this point a decision is made whether a low anterior resection is possible or an APR in necessary. If an APR is necessary the dissection continues below the luyatory ani muscles. The perineal dissection then begins and anal canal and lower rectum are dissected out through the ischiorectal fossa and the urogenital diaphragm. In an extensive tumor removal of vagina, vulva and urethra may be necessary. The specimen can then be removed abdominal or perineal incision. The reconstructive phase now begins.

**POSTERIOR EXENTERATION**

A posterior exenteration may be performed in a female if the bladder is not involved in the tumor. The vagina, cervix, uterus and adnexa are removed along with the rectum. The procedure is similar to a total exenteration, except instead of dissecting anterior to the bladder in the retropubic space, the peritoneum over the bladder is incised and the bladder is sharply dissected off the anterior surface of the cervix and vagina down to or beyond the levatory ani muscle depending on the level of the tumor. The ureters must be dissected free distally from the anterior parametria over the ureteral tunnel as it runs along with the uterine artery. APR and sacrectomy The operation begins in the same fashion as a total exenteration.

The anterior dissection is developed in the ventral plane preserving the female reproductive organs, prostate and bladder if possible. The dorsal and dorsolateral dissection follows the transsacral plane down to the level of the transsection of the sacrum. If the tumor extends up to the level of S2 the cancer is deemed unresectable.
At this stage the level of sacral transaction is marked using K-wire through the sacrum or a deep cut of the osteotome. A gauze can be placed in the presacral space to reduce bleeding while the patient is turned into the prone position. When the patient is in the prone position a dorsal longitudinal incision is made from L5 down to and incorporating the anal canal.

The gluteus maximus and minimus muscles are then dissected off the sacrum as flaps are raised bilaterally. The sacrotuberous and sacrosinous ligaments are transected at the sacrum which facilitates access to the pelvic floor muscles, and the infra piriformis opening. Medially to the infra piriformis a finger can be introduced into the presacral space to identify the level of the sacral resection. The sacrum is then resected with care taken not to damage the sacral roots. Then sacrum, the lateral pelvis walls and the rectum are then removed en bloc. If there are any concerns about inadequate tumor margins the area should be irradiated with intra-operative radiotherapy (IOERT) if it is available. Sacropelvic Exenteration. Sacropelvic exenteration combines the posterior dissection of the APR sacrectomy and the anterior dissection a pelvic exenteration.

This is reserved for patients with bulky rectal tumor extending into the sacrum posteriorly and the female reproductive organs or bladder and prostate. The rectum is removed en-bloc with the sacrum and resected visceral organs following division of the sacrum in the prone position. Again IOERT can be used if there is any doubt about an R0 resection APR/LAR with partial cystectomy of vagina. If the rectal tumor does not extend too aggressively into the bladder or specifically the trigone of the bladder, a partial cystectomy may be performed.

If necessary the ureters can be reimplanted using a psosas hitch reconstruction. Similarly if part of the vagina is involved a local resection of part of the vagina may be undertaken. If the vaginal defect is too large to be closed primarily a myocutaneous rectus abdominus flap may be used to reconstruct the vaginal defect.

PELVIC AND PERINEAL RECONSTRUCTION

The organs and areas which may need reconstruction include the bowel, bladder, vagina, and large perineal defects. If the external anal sphincters were able to be preserved a colorectal or coloanal anastomosis with or without a J-pouch or coloplasty may be performed. A covering defunctioning ileostomy would always be recommended due to the increase probability of an anastomotic leak due to the extensive surgery and neo-adjuvant treatment. If an APR is performed an end colostomy must be constructed.

The bladder if completely resected can be reconstructed using a variety of different techniques using colon or ileum leaving patients with continent (Indiana pouch, Mainz pouch, Florida pouch or Miami pouch) or incontinent (Ileal conduit, colonic conduit or ureterocolostomy) urinary diversions. The decision whether to use reconstructive flaps in closure of the perineal defect or to close primarily depends on the side of the defect left in the perineal wound. Should the vagina need reconstructing or the sacral resection performed then a myocutaneous flap, either with the rectus muscle of the gracilis muscle would be advisable to facilitate wound healing.

Omental patches and prosthetic and biological meshes or grafts have also been advocated to fill the pelvic dead space following extensive pelvic exenterations.

OUTCOME

The single most important factor influencing both local recurrence rates and overall survival is the ability to obtain a complete microscopic or R0 resection. Other factors affecting survival include the presence positive lymph nodes, lymphovascular invasion, and a lack of response in CEA level post-operatively. Overall survival rates for locally invasive rectal cancers are relatively good with 5 year survival rates ranging from 49% to 64% following pelvic exenteration and 47% to 68% following abdomino-sacral resections. (Tables 1 & 2)

SUMMARY

Patients with rectal tumors extending into adjacent organs now have potentially curative treatment options. Multi-modality treatment is the optimal therapy with neo-adjuvant radiotherapy and chemotherapy facilitating down staging of tumors, enabling less aggressive resections. Good pre-operative imaging with a high resolution MRI scan can allow planning of the appropriate surgical procedure and organ resection. Treatment options must be made in the setting of a multidisciplinary team including not only colorectal surgeons but gynecologists, orthopaedic surgeons, plastic and reconstructive surgeons, radiation oncologist and oncologists. Patients need to be psychologically prepared for extensive resections, prolonged hospital stays and high incidences of morbidity. Input from stoma therapy nurses, dietetics and pre-operative counseling is crucial to prepare patients for the rigor of treatment.

Following tumor resection and recovery, adjuvant chemotherapy is advisable to reduce the risk of local and distant recurrence. In conclusion, following multimodality treatment and extended surgical resection, 5 year survival of up to 60% can be achieved with acceptable patient morbidity.

SUMMARY

EKSTENZIVNA HIRURGIJA I PELVIČNA EGZEN- TEREZA KOD LOKALNO UZNAPREDOVALOG KAR- CINOMA REKTUMA. GDE SU GRANICE?

Istorijski, lokalno uznapredovalim karzinomima rectuma sa tumorskom invazijom u okolne organe (T4 N1,2 stadijum tumora) davan je loaša prognoza i tretrani su sa palijativnom namerom. Medjutim, uz napredek mul ti - modalne terapije, kao i hirurških rekonstruktivnih tehnika, ekstenzivne resekcije kod karcinoma rectuma sa prihvatljivim morbiditetom i odličnim onkološkim rezult atima.

Ključne reči: lokalno uznapredovali karcinom, rektum, resekcija
REFERENCES


