Giovanni Dapri
John H Marks *Editors*

Surgical Techniques in Rectal Cancer

Transanal, Laparoscopic and Robotic Approach

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Foreword 1

Perhaps it is providence that set the stage for the sea change in rectal cancer management that has occurred in the last decade. After nearly a century of relatively sparse production of new and acceptable scientific information regarding rectal cancer, the recent surgical revolution has changed everything. The explosion of interest and performance of minimally invasive surgery with the involvement of an entirely new breed of surgeons, youthful and energetic, has led to new and imaginative ways to accomplish surgical objectives. A small cadre of surgeons who focus their talents upon rectal cancer treatment has developed procedures that are beyond ordinary imagination. These methods are capable of reducing perioperative discomfort, increasing patient safety and curability while maximizing the preservation of normal sphincter function; and as a result these new methods, despite the technical challenge, are gaining traction in the surgical community. Based on a platform of neoadjuvant therapy that the surgical–oncologic world has accepted as beneficial, these new surgical techniques have become transformational.

With this backdrop of dramatic changes in rectal cancer surgery, this book, *Surgical Techniques in Rectal Cancer*, is timely and serves a powerful need. The book is also a celebration of the energy, creativity, courage, and pioneering spirit of the authors. This text is predicted to become a standard reference for contemporary cutting-edge comprehensive rectal cancer management. Rectal cancer's reputation among patients and surgeons alike as one of the most dreaded visceral neoplasms may diminish with the adoption of the surgical techniques and multidisciplinary treatment plans described in this text. Having spent almost seven decades in search of better ways to treat rectal cancer, I have the distinct privilege and honor to offer this commentary and to salute the author heroes who through their talents and new ideas have provided new hope and promise for the rectal cancer patient.

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Foreword 2

There has never been a time in coloproctology when there are so many "known unknowns." This book brilliantly sets out to update us on each of them and to inform us of where each new technology stands in the spectrum of our specialty. In a book so dazzling with new technology for surgery and endoscopy, it is good that the first great "known unknown"—the Complete Response—is given the priority it deserves. I believe that it is now urgent for the profession to recognize that a pathological complete response (pCR) on a histology report after major surgery usually represents one or more errors of judgment or communication by the attending physicians. In their hands a major technological achievement has been reduced for the patient to a truly "hollow victory." That there should be a whole chapter on the management of such cases by surveillance is testament to the balanced editorship of this volume. All the old-fashioned human skills and ability to communicate with the patient are challenged in the face of this new "known unknown."

The year 2016 is indeed a battleground for so many new technologies. Many patients have been led to believe that a robot performing their operation will be superior to a human. Patients need to understand that a bad surgeon with the very best robot is a bad choice when compared with a good surgeon with the instruments of yesteryear—sharp long scissors, the St. Marks retractor, a good light, and the "Patience of Job." Nevertheless, the future will belong to the surgeon who takes those same qualities and applies them with all the advantages of magnification, superior vision, the best diathermy, the ligasure, and all the panoply of aids to modern precision and hemostasis. He will certainly win the everlasting battle for the best outcome.

So many new technologies also threaten the patient with the "hammer and nail" syndrome—if the only tool you have is a hammer the world becomes populated with nails! Throughout medicine the super-specialist with one procedure needs restraint: "because it can be done is not necessarily a reason for doing it!" Another old-fashioned skill required of the attending physician is that of the broker who puts the patient into the right hands.

All the new technologies require patience, skill, and practice, and the specialist colorectal unit of the future will need a wide menu of available alternatives. Laparoscopy, robotics, and endo-luminal tools of the future—all will be needed along with an improved anatomical grasp of the fascial layers of the pelvis, a keen pursuit of the neuro-anatomy of sex and continence—all these will need to be

combined with recognition that "practice makes perfect." Sadly, as Sir Edmund Hillary of Mount Everest fame said, "If it is more difficult it will be done worse by some." Teaching, auditing, peer review, and a willingness to accept criticism and improvement—all these mean that the impending struggle between technologies needs to be backed by great skill, hard work, and humility from the surgeons of the next generation. For coloproctology "know-how" they can start by reading this book.

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Preface

In the last century, the treatment of rectal cancer has been predicated on an abdominoperineal resection (APR). The last decade has seen an explosion of alternatives for rectal cancer specialists to use for the cure of their patients. Widespread use of neoadjuvant chemoradiation, total mesorectal excision (TME), transanal abdominal transanal surgery (TATA), and minimally invasive surgery (MIS) have allowed for the expansion of sphincter preservation and greater cure for the rectal cancer patient. The merger of these approaches has promoted an emphasis on both curing the cancer and maximizing the quality of life.

However, while an impressive multitude of options are now available, the quantity of techniques coupled with the variety of technology and the judgment required to offer an individualized treatment for the rectal cancer patient can leave both the beginning surgeon and the experienced practitioner at a loss as to how best to proceed.

This book has been created to offer the clearest explanation and description of the most cutting-edge options available to treat rectal cancer. Starting with the introductions by Bill Heald, the father of TME surgery, and Gerald Marks, a pioneer in sphincter preservation after radiation therapy and TATA, the 32 chapters have been assigned to an all-star cast of worldwide pioneers in rectal cancer. Each chapter has been written with care and precision to offer to the reader an emphasis on the critical technical points as well as the major take-home messages. The clarity of the text is enhanced immeasurably by the numerous figures and illustrations, permitting complete understanding of each surgical technique from its beginning until the final step.

The two forewords, offered by giants in the field, introduce the reader to the tremendous content of this book. The organization of the book was created to take the reader from presentation of the cancer, through the essential anatomy, neoadjuvant treatment options, and then to the operating room.

This book on rectal cancer has been divided into three main parts: I. History, Anatomy, Evaluation and Medical Treatment; II. Abdominal Laparoscopy and Robot-Assisted; and III. Transanal Laparoscopy and Robot-Assisted.

The book has been written to be useful for everyone involved in rectal cancer management. From internists, gastroenterologists, endoscopists, oncologists, radiotherapists, and radiologists involved in the treatment of rectal cancer during their daily practice, to surgeons specialized in colorectal surgery, to junior faculty, to trainees all interested in new and innovative techniques, this book is for you. We hope you enjoy it!

Giovanni Dapri

John H Marks

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Part I

History, Anatomy, Evaluation and Medical Treatment

1 History of Rectal Cancer Surgery

Sharaf Karim Perdawood

Abstract

The surgical treatment of rectal cancer is very challenging and is one of the most rapidly advancing. At this time, different varieties of treatment options exist and new surgical methods are being explored. Thanks to numerous great pioneers in colorectal surgery in the last century, surgery for rectal cancer has changed from being purely palliative to one that made this solid malignancy a curable disease in the vast majority of cases. The evolution path has started few centuries ago, with early efforts to relieve symptoms by limited excisions. With the evolvement of general anesthesia, more extensive resections were made possible and different approaches could be tried. With the accumulation of experience, tumor removal could be combined with conservation of bowel continuity, an option which was not possible earlier. Advances in the understanding of the pathophysiology of rectal cancer, has led to increasing chances of cure through adoption of different surgical principles. However, rectal cancer is still challenging and its treatment options continue to evolve. This chapter focuses on some important landmarks in the surgical treatment of rectal cancer and on some of those pioneers who have contributed to it and to shape the modern rectal cancer surgery.

Keywords

Rectal cancer • History • Surgery

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1.1 Stomas

Colorectal surgery is inseparable from stomas, thus studying the history of rectal cancer surgery necessitates knowledge of the history of stomas. This is as ancient as history of abdominal trauma, in which "stoma" was an inevitable result of. A clear reference to this is found in the Bibel, describing Eglons belly after being stabbed by Ehud "Even the handle sank in after the blade, and his bowels discharged. Ehud did not pull the sword out, and the fat closed in over it" [1]. For centuries, purposeful stoma formation was advocated to treat abdominal traumas and bowel obstruction. The later often due to incarcerated hernias or tumors, including obstructing rectal cancer. While evidence of stoma creation to relieve bowel obstruction can be found in the writing of the Greek Praxagorus in 400 B.C. "…he (an unknown doctor) seemed to be a very bold practitioner for in this distemper (bowel obstruction) if the remedies did not operate, he ordered an incision to be made into the belly and even into the gut itself and the excrements to be drawn out and the wound sewed up again" [2], the history does not tell us much about purposeful stoma formation until the beginnings of the eighteenth century.

In 1710, Alexis Littré suggested stoma creation for imperforated anus [3]. One of earliest reports of stoma creation to treat obstructing rectal cancer is by Daniel Pring, an English surgeon who performed a lumbar colostomy [3], a procedure which was invented by the Danish surgeon Duret Callisen [4], and later developed by Jean Zulema Amussat [3]. Being regarded as a palliative measure for many decades, the importance of stoma creation increased with the advances in the surgery for rectal cancer.

1.2 Perineal Approach

The first description of signs and symptoms of rectal cancer was made by the English surgeon John Arderne as early as in 1376 [5]. Rectal resection was, however not done until 1793, when Jean Faget performed the first ever mentioned rectal resection. The procedure was done for an extensive ischiorectal abscess, which appeared to be a perforated rectal cancer [6]. The procedure was, thus not planned to treat cancer. In the nineteenth century, the French surgeon Jacques Lisfranc performed the first planned rectal resection for cancer. This was done in 1826 in the pre-anesthetic era. Lisfranc's resection was a very limited one, composed basically of a wide local excision by removing the lower part of the rectum. In his paper which was read before the Academic Royale de Medecine 5 years later, he reported his initial results in nine patients. Six of these patients has survived and albeit surprisingly almost continent [7]. Similar procedures were performed in England by Hubert Mayo of the Middlesex Hospital in 1833, and James Wardrop in 1834 [8]. In Germany, Johann Dieffenbach reported a similar operation in 30 cases, all survived and were probably disease free for a year [9]. At that time, rectal cancer procedures were mostly palliative and with this perineal approach, exposure was very limited, allowed only the lowest part of the rectum and the anal canal to be removed.

1.3 Posterior Approach

With the advent of anesthesia, it became easier to operate and more extensive resections could be performed. Of particular interest is the change in the operative technique for rectal excision, which took the form of removal of the coccyx. This has served as a measure that could allow for more extensive excisions and more effective drainage of the blood which was particularly a problem at that era, due to lack of effective intraoperative hemostatic measures. One of the pioneers, who have contributed to the spread of coccyx removal was Verneuil, who in 1873 and encouraged by the French surgeon Jean Zulema Amussat, excised the coccyx to extend the limits of excision [10]. Theodore Kocher in Germany (Fig. 1.1) also adopted coccyx excision in 1874 [11].

While these advances were adopted by increasing number of surgeons, these excisions could be criticized due to the dangers of bleeding, sepsis, and incontinence. The English surgeon Thomas Curling of the London Hospital and President of the Royal College of Surgeons (Fig. 1.2) wrote in 1876: “Excision of the carcinomatous rectum was practiced formerly by Lisfranc and Dieffenbach and is

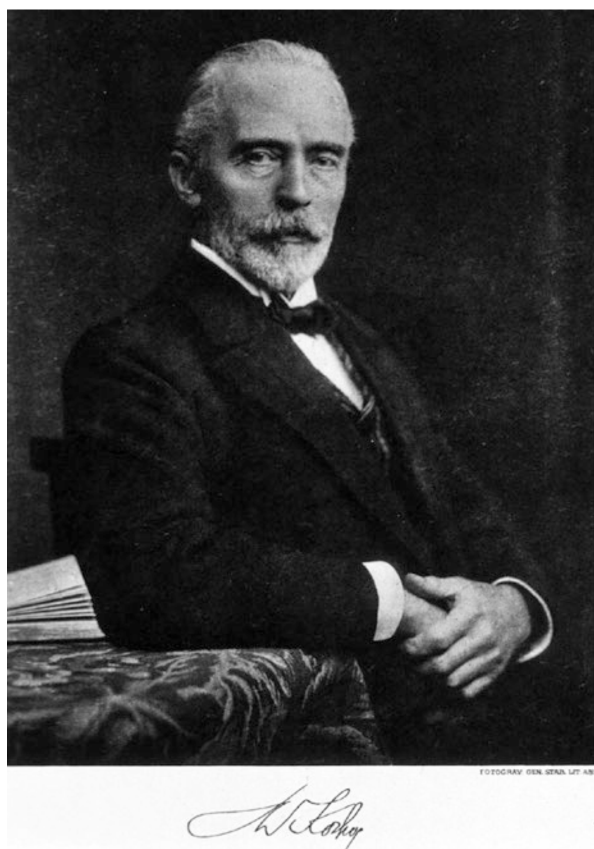

Fig. 1.1 Emil Theodor Kocher (1841-1917)

Fig. 1.2 Thomas Blizard Curling (1811–1888)

resorted to in the present day by several German surgeons. I am unwilling to discourage any attempt to relieve so dire a disease as cancer of the rectum, but knowing the danger that must be incurred from haemorhage in the operation, the misery likely to ensue from incontinence of faeces as well as the prospect of early return of the disease, I cannot think that a chance even of a prolongation of life is worth acceptance on the terms offered of such an operation" [12]. Despite critics from Curling and other contemporary surgeons, increasing number of rectal excisions were performed. In 1876, William Harrison Cripps presented 53 cases operated between 1826 and 1875. The mortality rate was 20% and it seemed that survivors had their lives prolonged, the incontinence was not "too high." The main cause of death was peritonitis.

Another landmark in the history of rectal excision is the popularization of transsacral approach by the German surgeon Paul Kraske (Fig. 1.3). He was at a time Director of the Clinic at Freiberg, and after practicing the approach described by Kocher, he wanted to have a better exposure for lesions higher up in the rectum as well as to achieve a better control of hemorrhage [11]. Kraske made a new posterior approach removing the coccyx and part of the sacrum as well. His results in two patients were read to the 14th Congress of the German Society of Surgeons in Berlin 1885. This new approach was probably not standardized and even Kraske himself was not performing it the same way every time. Transsacral approach has afterwards flourished and various surgeons adopted it, usually adding their own modifications, like Julius Hochenegg who brought out the upper cut end of the bowel through the anus (pull through technique).

Fig. 1.3 Paul Kraske (1851–1930)

Due to the mutilating nature of these approaches, attempts to find better and less invasive methods continued. One of the controversial approaches is the transvaginal approach. A.T. Norton described in 1889 a transvaginal resection with the reestablishment of continuity and postoperative continence [13]. William Heath Byford (Fig. 1.4) performed a transvaginal resection, combined with excision of the posterior vaginal wall and sutured both ends of the bowel to the vaginal defect. He then closed the vaginal introitus, and has maintained bowel continuity [14]. Another modification of this transvaginal procedure with utilization of the vaginal lumen is the method advocated by L. L. McArthur [15]. He used the vaginal lumen to replace the excised rectum, and claimed that the patient was continent. Byford postulated the following advantages of the transvaginal approach: replacement of the excised rectum by vagina, excision of as high tumors through this method as in transsacral approach with less trauma for the patient, exploration of the peritoneal cavity prior to resection itself and lastly, the procedure could be aborted and could end as a diagnostic procedure without much trauma for the patient.

Fig. 1.4 William Heath Byford (1817–1890)

1.4 Abdominoperineal Excision

The first surgeon who performed a combined abdomino (anterior)—perineal (posterior) excision for rectal cancer is the German surgeon Vincent Czerny (Fig. 1.5) in 1883. The procedure was probably done merely by chance, as it was planned as a routine transsacral approach for a high rectal cancer. However, it seems that Czerny was unable to complete the procedure through a transsacral route for some reason. He then simply turned the patient to a supine position and completed the procedure by transabdominal approach. The operation was, however unsuccessful in terms of patient survival [16]. Nonetheless, this accidentally performed procedure marks a new era in the surgical treatment of rectal cancer in terms of being able to do a synchronous abdominoperineal rectal resection.

At the end of the nineteenth century and the beginning of twentieth century, abdominoperineal excision was performed in a way that the rectum was removed as a tube without mesorectum and without removing the lymphatics. At the same time, a growing attention was paid to local disease recurrence. Early results of that kind

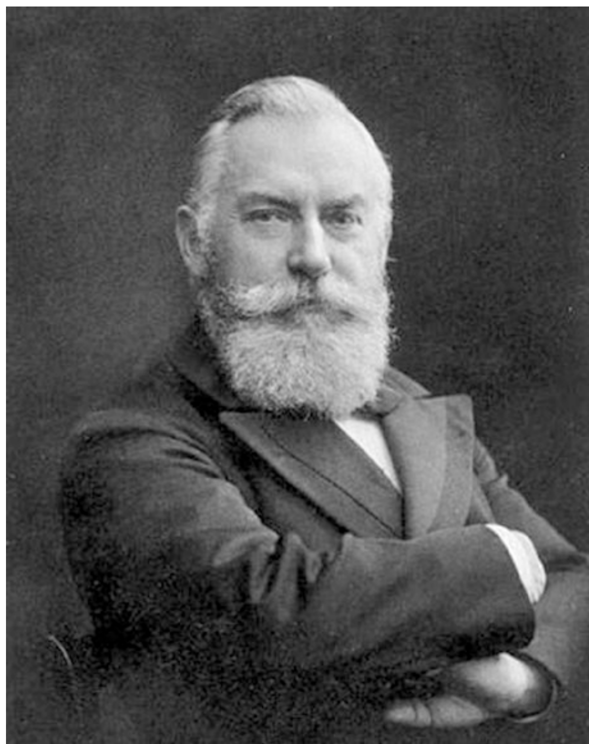

Fig. 1.5 Vincenz Czerny (1842–1916)

of surgery showed very high recurrence rates (Table 1.1). It was during that period where one of great pioneers of rectal cancer surgery appeared on the scene, represented by the English surgeon Ernst Miles, who was appointed assistant surgeon at the Royal Cancer Hospital. Miles had similar high recurrence rates as his contemporary surgeons. After performing autopsy on his own patients who died from recurrence, he invented a new approach. According to Miles, those very high recurrence rates were due to insufficient removal of tissue and thus attention needed to be paid to the lymphatic spread of cancer. He adopted a wide "cylindrical excision" to include lymphatics in the removed rectal specimen. Miles published his first results after performing this extensive excision in 1908 [17]. A similar observation and a similar new method of excision were done by Charles Mayo (Fig. 1.6) [18]. The procedure was associated with high mortality in the early period of adoption although it appeared, on the other hand, that the oncological results were improving dramatically. One of early adopters of Mile's operation was JP Lockert-Mummery, a senior surgeon in St. Mark's Hospital. He had at that time, introduced several modifications of the existing operations. He considered that Mile's operation was associated with high mortality and modified it as well.

While an extended abdominoperineal excision became a reality with obvious benefits in terms of improved oncological quality, concerns began to rise further about the mutilating nature of the procedure and ways to minimize complications, as well as selection of patients for whom a less invasive procedure would be satisfactory.

Table 1.1 Some oncological results of rectal cancer surgery in the beginning of the twentieth century

Surgeon	Number of patients	Recurrence rate (%)
Allingham	18	100
Cripps	85	38
Vogel	1500	80
Miles	57	95

Fig. 1.6 Charles Horace Mayo (1865–1939)

1.5 Hartmann's Operation

Hartmann's operation involves resection of the sigmoid colon and/upper rectum, closure of the remaining rectal stump and fashioning a colostomy. It is performed nowadays mainly for the surgical treatment of diverticulitis. The idea of preserving the distal part of the rectum not involved by cancer came from the need to reduce morbidity and mortality associated with abdominoperineal excision. The first procedure of this art was probably performed by the Austrian surgeon Karl Gussenbauer (Fig. 1.7) in 1879 [19]. The French surgeon Henri Albert Hartmann (Fig. 1.8), who was once professor of surgery at Hotel Dieu in Paris, has later popularized the procedure. This has probably happened between 1909 and 1923 [20], and the procedure ended up bearing Hartmann's name when some unknown surgeon in the 1930s performed a two-staged procedure of sigmoid resection and colostomy with anastomosis at the second stage.

Fig. 1.7 Karl Gussenbauer (1842–1903)

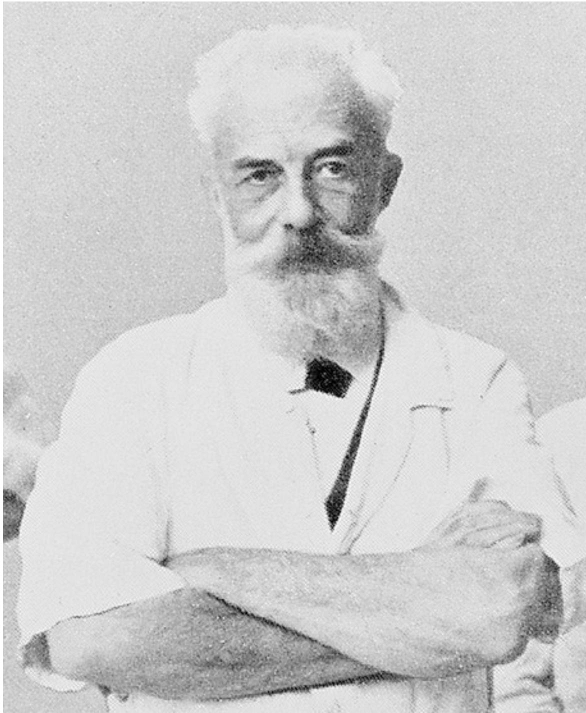

Fig. 1.8 Henri Albert Hartmann (1860–1952)

1.6 Sphincter Preservation

At the beginning of twentieth century, Mile's abdominoperineal excision reached a state of standard surgical procedure for excision of rectal cancer, regardless of tumor height from anal verge. Needless to say, this was mutilating and for patients with high rectal cancers, its necessity was doubtful. The main disadvantage was the need for permanent colostomy. In 1910, the first attempt at performing anastomosis was described by the American surgeon Donald Church Balfour. He performed an abdominal rectal resection and an end-end anastomosis [21]. Balfour's method, which included the use of a tube to support the anastomosis, had a very high anastomotic leak rate and did not gain popularity. Furthermore, at that time where Mile's extensive excision has convinced surgeons due to its oncological benefits, preservation of some distal part of the rectum to perform the anastomosis, was concerning and even not oncologically correct, as formulated by William Mayo (Fig. 1.9) "the operation is probably not radical enough" [22].

However, thanks to the extensive research by Dukes who could demonstrate the safety of sphincter preservation, efforts continued to limit the resections and preserve sphincters. Dukes showed that the lateral and downward spread of cancer was overestimated by Ernst Mile's, as downward lymphatic spread appeared to be the case in only a minority of patients with advanced disease [23]. In 1951 Goligher et al. [24] analyzed 1500 rectal specimens and found that the distal spread of tumor

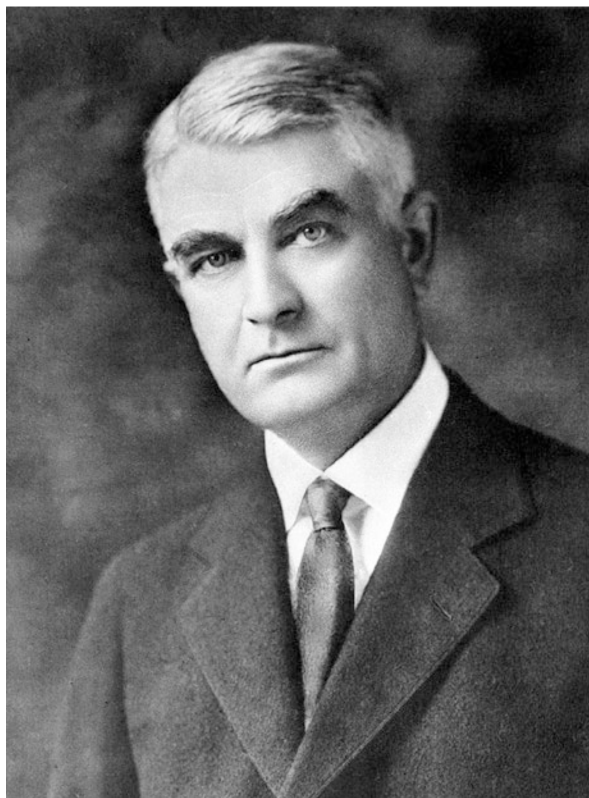

Fig. 1.9 William James Mayo (1861–1939)

cells more than 2 cm did not exceed 2%. A safety margin of only 5 cm could therefore be considered enough to achieve radicality.

Ultimately, the safety of sphincter preservation could be established by Claude Dixon of Mayo Clinic in 1948. He could demonstrate an impressive 5-year survival rate of 64% among 400 patients, results he presented at the meeting of the American Surgical Association in Quebec, Canada [25, 26]. Thus, Mile's theory was rejected and anterior resection became the standard of care for the treatment of mid and upper rectum cancer. Abdominoperineal excision, on the other hand came to stay for many years including present time, in the treatment of lower lesions. While the general believe was that an adequate resection required at least 5 cm distal resection margin, research results showed that lymphatic spread was limited to the level of the tumor or higher up. What encouraged the preservation of the sphincters was the increasing number of papers that showed even a distal margin of 2 cm did not compromise the oncological safety [27]. In the late 1970s, an almost radical shift from abdominoperineal excision to anterior resection is observed.

While preserving the anal sphincter appeared to be safe, another challenge was to actually perform the anastomosis. A positive innovation enabled a shift from the technical difficulty of performing a hand sewn colorectal or coloanal anastomosis, to a smarter way represented by the use of circular stapler devices. The circular

devices were developed by Russian surgeons. The breakthrough in the use of staplers happened in 1972 when the American surgeon with a Russian born father, Mark Mitchell Ravitich could be introduced to one of hand-crafted staplers during his visit to Kiev in 1958. He could take one of these devices back to the USA. Several years later, staplers were widely available [28].

1.7 Total Mesorectal Excision

Throughout the first seven decades of the twentieth century, surgery for carcinoma of the rectum has evolved from being a limited transanal or transsacral excision, to a wider excision with unnecessary removal of an extensive amount of tissue of the rectal wall and its surroundings. This has yielded oncologically superior results as expected. However, it seems that with the rejection of Ernst Mile's theory of downward lymphatic spread, the procedure returned almost to the original description with mere removal of the rectal tube. This was the case for surgeries involved anterior resection, which included a blunt dissection in the pelvis, leaving inevitably the mesorectum and endangering the oncological safety. Recurrence rates were high at the end 1970s, when the English pathologist Phil Quirke has renewed the interest for the lateral lymphatic spread in the mid-1980s. He found a correlation between an involved radial resection margin and the development of local recurrence and poor survival [29]. This was a call for action, to improve the quality of rectal cancer surgery.

The English surgeon RJ (Bill) Heald has, since 1982 contributed for the major change in the principles of rectal dissection. He could show improved local recurrence rates through invention of a new resection technique that ensures complete removal of the mesorectal envelope. Surgical planes in Heald's Total Mesorectal Excision are defined embryologically, as the mesorectum has a separate embryological origin than the surrounding tissue. The technique involved a complete removal of the rectum together with the mesorectum down to the levator muscles, through a sharp and precise dissection and a gentle traction avoiding breach in the mesorectal envelope [30–32]. Heald could demonstrate a dramatic improvement in 5-year disease-free survival from around 50% at that time to an impressive 80% and showed local recurrence rate of only 4% [33]. Total Mesorectal Excision has become the gold standard for removal of mid and low rectal cancers in most parts of the world.

The improved oncological outcomes after the introduction of TME were not the only point of focus. Life quality issues, genitourinary function and the importance of nerve preservation have all gained significant amount of attention and research still ongoing to identify ways of improving functional results after rectal cancer surgery.

1.8 Lateral Lymph Node Dissection

In Japan, a more extensive procedure to achieve local tumor control has been advocated for, the so called lateral lymph node dissection [34–36]. The principles of this technique were described in 1950s by Deddish [19] and Bacon [37]. The procedure is not considered a standard of care in the western countries due to several reasons, amongst which the high rates of complications especially nerve damage leading to

urogenital dysfunction. Furthermore, more blood loss, longer operation time, and the fact that it may represent a sign of distant tumor spread has discouraged colorectal surgeons to indulge into this practice.

1.9 Laparoscopic and Robotic Surgery

Laparoscopic surgery for rectal cancer was reported for the first time in 1990s [38]. With its obvious advantages like less blood loss, and shorter recovery, laparoscopy has gained its place as a standard method in colorectal surgery. Laparoscopic surgery for colorectal cancer is, at this time widely implemented in the Western world, especially in Europe. The pathological results are more controversial, with several major trials demonstrating contradicting results of laparoscopic rectal cancer surgery compared with open technique [39–41].

Robotics are being increasingly used in the recent years, with promising first experiences [42]. The main arguments for their use in rectal surgery are better visualization with three-dimensional cameras and angulated instruments providing better ergonomics for the surgeon. Thus potential advantages are lower conversion and better preservation of urogenital function. The proof of superiority over laparoscopic surgery is, however lacking. Robotic rectal resection has been otherwise shown to be safe and feasible [43–45]. Robotic rectal resection takes longer time, probably due to longer preparations needed to start the procedure and the subsequent steps not directly related to dissection itself [46]. The real benefits of robotic rectal resection are to be proved through randomized controlled trials, and the results of one such are being awaited to be published [47].

1.10 Transanal Procedures

In the early 1980s, Total Mesorectal Excision was reported and began to gain widespread interest. Simultaneously, in 1983 the German surgeon Gerhard Friedrich Buess introduced a new procedure for the treatment of benign rectal lesions. The method as based on a transanal local tumor excision, thus avoiding major surgery. He called the procedure Transanal Endoscopic Microsurgery (TEM) [48]. The interest for local excision of early rectal cancer has been growing, especially with advances in chemoradiation and the implementation of screening colonoscopies for colorectal cancer and the expected increase in the detection of higher number of early rectal lesions.

In the recent years, transanal endoscopic surgery has gained enormous interest due to its potentials, not only in local excisions, but in rectal resections as well. Through a transanal approach, a potentially better view of the most difficult part of the anatomy could be achieved allowing for a more precise and safe procedure. Transanal or perineal dissection has been shown to be feasible and safe [49–51]. The procedure has evolved from dissection without instruments [52], to the use of transanal endoscopic ports which allowed that Total Mesorectal Excision to be feasible in both cadaveric series [53], as well as human series. The first reported case of transanal TME in a patient using transanal port was reported in 2010 [54]. There

are numerous publications in the years followed that, showing that transanal TME is feasible with potentially several benefits.

The future of rectal cancer surgery will definitely follow the same path as its history, with focus on more radical approaches through less invasive methods. One thing is for sure; the job is not done yet, and the history of rectal cancer surgery will not stagnate.

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Epidemiology and Carcinogenesis of Rectal Cancer

2

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Abstract

Cancer of the colon and rectum is extremely common in the Western hemisphere. The etiopathogenesis of colorectal cancer is an intertwined play of several genetic and environmental factors to which an individual is exposed to during the lifetime. The predominance of one factor over another decides the timing of development of this cancer with respect to the individual's age. Familial syndromes like Lynch syndrome and familial adenomatous polyposis predispose an individual to cancer early in their lifespan since they carry the genetic mutation. A sporadic cancer, on the other hand, follows a very interesting and often predictable path from a polyp to carcinoma. There are three such pathways which the colonic epithelium may undertake toward the development of cancer. Each of the pathways has its own unique set of genotypic and phenotypic expression which needs to be understood well to accomplish our ultimate goal for prevention of colorectal cancer.

Keywords

Colorectal cancer • Epidemiology • Lynch syndrome • Carcinogenesis • Polyp-carcinoma sequence

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