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Historical Perspective

The Wertheim hysterectomy: Development, modifications, and impact in the present day

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HIGHLIGHTS

- Wertheim's radical abdominal hysterectomy technique is outlined.
- Major modifications to the Wertheim hysterectomy are discussed.
- Modern modifications focused on quality of life are examined.

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ABSTRACT

Ernst Wertheim was a pioneer in the history of the surgical treatment of cervical cancer. His English-language manuscript “The extended abdominal operation for carcinoma uteri (based on 500 operative cases),” which was published in 1912, detailed his standardization of the radical hysterectomy and formed the basis of the current treatment for early stage cervical cancer. We contextualize the Wertheim hysterectomy, emphasizing medical advances that allowed for its development and subsequent modification. We then discuss modifications to the originally proposed procedure, including a maximally extended parametrial resection pioneered by Takayama, and the addition of the Taussig en bloc lymph node dissection by Meigs, both of which afforded an improved mortality profile due to decreased disease recurrence. Finally, we discuss progress that has been made in the present day, such as the development of nerve-sparing and fertility-sparing surgeries, as well as the introduction of the robotic platform. In this way, we hope to provide a historical background for the Wertheim hysterectomy—a cornerstone of gynecologic oncology.

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1. Introduction

In 1912, the Austrian surgeon Ernst Wertheim published a landmark English-language manuscript in the *American Journal of Obstetrics and Diseases of Women and Children*, in which he detailed 500 cases of what he termed “extended abdominal operation for carcinoma uteri,” now widely known to the gynecologic community as the radical abdominal hysterectomy (Fig. 1) [1,2]. Since that time, remarkable progress has been made in the surgical treatment of cervical cancer—a disease considered foolish to attempt to cure as recently as one century

ago. Yet, as our understanding of disease processes and surgical techniques expands, it is befitting to consider the context in which our modern advances have arisen.

In standardizing the radical abdominal hysterectomy, Wertheim took the first necessary step toward the development of a safe and feasible operation for the treatment of locally invasive cervical cancer—an undertaking equally rooted in surgical technique and management of operative morbidities. As the century progressed, availability of antibiotics and blood transfusion triggered sharp declines in perioperative morbidity and mortality, and Wertheim's operation became increasingly commonplace, permitting its modification in pursuit of greater survival benefit. As survival rates improved, focus gradually shifted toward improving post-surgical quality of life. In the following discourse, we attempt to contextualize the pioneering work of Ernst

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ORIGINAL COMMUNICATIONS.

THE EXTENDED ABDOMINAL OPERATION FOR CARCINOMA UTERI.

(BASED ON 500 OPERATIVE CASES)

BY
PROF. DR. E. WERTHEIM,
Vienna.

(With Six Illustrations.)

Translated by
HERMANN GRAD, M. D.,*
New York.

A. THE DEVELOPMENT OF THE TECHNIC OF THE OPERATION.

From the beginning it has been clear that in order to obtain good results in the extended *abdominal operation for uterine cancer* the development of the technic was of great importance. Careful *asepsis*, rapid completion of the operation, a minimum loss of blood, careful handling of the organs to be liberated and the consideration of the heart in reference to the narcosis; all these points are of great moment in an individual already reduced in strength by the disease. We are, therefore, not in accord with Rosthorn,† who wishes to set aside the technical details with the remark that this operation should be carried out according to the idea of the individual operator. That other operators

* The remarkable results obtained by Professor Wertheim in his radical operation for cancer of the uterus have aroused great interest in his technic. For the benefit of his English-speaking admirers a translation of his recent work is here presented, its publication being authorized by Professor Wertheim. It is regretted that lack of space prevents the publication of the 500 detailed case reports upon which the Monograph is based.
† *Zentralbl. f. Gyn.*, 1901, No. 11.

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Fig. 1. Cover page of Wertheim's 1912 manuscript.

Wertheim and delineate the intricate history of the radical abdominal hysterectomy, highlighting along the way the major advances in the operations now routinely performed in operating suites worldwide.

2. Development of the Wertheim hysterectomy

The development of successful surgical treatment for cervical cancer faced distinct challenges—namely perioperative infection and blood loss—in an era before the availability of antibiotics and blood transfusion. In an effort to address the need for surgical treatment for patients with gynecologic malignancies, abdominal hysterectomies had been attempted, though with poor success. Perioperative mortality rates averaged 75–80%, leading experts to recommend the procedure only for patients in dire clinical situations [3]. In 1878, Wilhelm Alexander Freund proposed a standardized technique for total abdominal hysterectomy, taking the first steps toward the development for safe, feasible operations for gynecologic malignancy [4]. Despite still-significant surgical mortality and the realization soon thereafter that the total

abdominal hysterectomy provided no significant survival benefit to patients with invasive cervical cancer, Freund's standardization of this procedure undeniably laid the groundwork for development of the radical hysterectomy.

Extrapolating William Halsted's 1889 proposal that en bloc resection of uninvolved tumor-surrounding tissues could prevent breast cancer recurrence, John Clark and Emil Ries, gynecology residents at Johns Hopkins University, proposed the resection of not only the cervix, but the uterine corpus, fallopian tubes, and a portion of the parametrium, and in so doing, undertook the first attempt at radical hysterectomy for cervical cancer in 1895 [4]. As the idea of radical hysterectomy took root in Europe and America, a famous rivalry regarding the optimal surgical approach to the radical hysterectomy developed between Friedrich Schauta and his protégé Ernst Wertheim at the Universitäts Frauenklinik in Vienna, Austria [5]. This rivalry culminated in Wertheim ultimately leaving his mentorship under Schauta for the Elizabeth Hospital in 1898. Wertheim went on to refine his technique, publishing a report of his first radical abdominal hysterectomy later that year, and in so

doing, developed the procedure that would come to be recognized as definitive treatment for carcinoma of the cervix [5].

In 1912, Wertheim published the English-language translation of his first 500 cases of radical abdominal hysterectomy, comprising 62 pages in which he highlighted his meticulous operative technique, intra-operative and post-operative challenges, as well as a retrospective analysis of 5 years of patient data [1].

Several hallmarks of Wertheim's operative technique allowed him to address challenges inevitably encountered by those attempting to undertake this operation. With regard to perioperative mortality, Wertheim noted that "careful asepsis, rapid completion of the operation, a minimum loss of blood, careful handling of the organs to be liberated, and the consideration of the heart in reference to the narcosis; all these points are of great moment in an individual already reduced in strength by the disease." Citing peritonitis as a major risk for mortality, Wertheim advocated curettage and cauterization ("paquelinization") of the carcinomatous focus prior to beginning the abdominal operation, with the goal of reducing bacterial seeding of the peritoneum from oft-infected tumor tissue. Likewise, Wertheim staunchly defended his abdominal approach, which he argued allowed for extensive work to be done in the abdomen prior to encountering diseased tissue. He was adamant that incision of the vagina be the final step before removal of the specimen (in stark contrast to the radical vaginal hysterectomy pioneered by his rival and former mentor Friedrich Schauta). Additionally, he noted that special curved clamps were fashioned for the purpose of clamping the vaginal tube, which allowed for facile containment of the carcinomatous focus and removal of the vaginal wall. Regarding wound care, Wertheim noted that he drained the peritoneum through the vagina only in cases where "pus [was] spilled, raw surfaces [were] left behind, or where there [was] danger of bowel perforation." In these circumstances, he placed iodoform gauze through the vaginal cuff into the peritoneum or sub-peritoneum for drainage, with great care taken to avoid pressure on the ureters for fear of necrosis and fistula formation [1].

Likewise, excessive blood loss was another cause of major operative mortality, and was cited by Wertheim as the "most difficult of the problems of the radical abdominal operation." To this end, Wertheim first attempted ligation of the internal iliac arteries, but soon found this to be of little use. Subsequently, he employed the use of parametrial clamps, which provided for easy ligation of vessels, and prevented the majority of bleeding typically encountered during his operation [1].

Regarding post-operative morbidity, the most common complication cited by Wertheim was post-operative urinary retention, which he referred to as an "unavoidable evil." In an attempt not to exacerbate the inevitable urinary retention experienced by his patients, he advocated loosening the bladder in three steps: the middle portion immediately upon entry into the abdomen, the lateral portions once the ureters had been freed down to the bladder, and the base of the bladder from the vagina with rounded scissors prior to vaginal incision. Wertheim urged the utmost caution in releasing the bladder, with the knowledge that careless treatment of this organ would result in prolonged postoperative urinary retention [1].

Similarly, ureterovaginal fistula comprised an infrequent, but severe complication of Wertheim's radical abdominal hysterectomy. Though resolute that the ureters must be liberated prior to attempting to extirpate the specimen, Wertheim readily acknowledged that their damage via kinking or severance would likely result in fistula formation. In an effort to avoid damaging the ureters, Wertheim proposed first locating them as they traveled through the posterior leaf of the broad ligament by bluntly dissecting the anterior and posterior leaves with a finger. Once the ureter was located on the posterior leaf, it was followed (again by bluntly dissecting with a finger) through the parametrium until the uterine vessels were encountered, ligated, and cut. The vesical portion of the ureter was then followed in the same manner until finding its junction with the bladder. Wertheim proposed that this technique of blunt dissection spared the ureteral sheath, and in so doing,

left the feeding vessels undisturbed and avoided necrosis and fistula formation. While only 32 patients (6.4%) developed ureterovaginal fistulae, and the majority of these healed spontaneously, Wertheim noted the worrisome implications of a fistula that failed to heal. Without antibiotics available, ascending infection would soon compromise renal function. Wertheim noted the need in these cases to intervene surgically, either by re-implanting healthy ureteral tissue into the bladder or performing nephrectomy [1].

Wertheim likewise urged caution in the treatment of the rectum. The rectum, he stated, was easily injured if the rectovaginal space was not sufficiently developed prior to attempting to extirpate the specimen. With his meticulous approach of incising the peritoneum at the junction of the fixed and mobile portions of the rectum and subsequently using a finger to push through the loose cellular tissue separating the rectum and vagina, the rectum was rarely harmed (0.4%). In the rare cases in which the bowel was perforated, it was immediately closed with suture with no lasting effects. Wertheim made mention of rare rectovaginal fistula formation, all of which healed spontaneously [1].

Particularly noteworthy was Wertheim's treatment of regional lymph nodes, which he removed only if found to be palpably enlarged. He advocated searching along the external iliac, internal iliac, and obturator vessels, as well as in the sacral region for palpable nodes, noting that even nodes that were small in size could have palpable features consistent with carcinomatous invasion. He states that some of his contemporaries favored a removal of the entire lymphatic system, to which he replied, "first of all, this could not be accomplished, and second, it is not necessary to do so" [1]. Controversy over this statement lasting nearly 40 years would fuel a major modification of the operation (Meigs), resulting in incontrovertibly greater survival benefit.

Regarding outcomes, in this series of 500 patients, Wertheim reported operability of 50%, overall mortality of 18.6% (largely due to peritonitis), and boasted an "absolute accomplishment" of 18.4% - a measure of all patients alive and free of disease recurrence at 5 years [1]. These figures would form the standard to which all other surgical approaches were compared for decades to come.

3. Subsequent modifications of the Wertheim hysterectomy

In 1911, the Japanese surgeon Shouhei Takayama began reporting radical abdominal hysterectomies performed in the tradition of Wertheim, but with particular attention paid to a maximally extended resection of the parametrium [6]. While Wertheim did not specify boundaries of parametrial resection in his manuscript, Takayama felt that Wertheim's operation did not achieve adequate parametrial resection, thus hampering the attainment of maximal operability. By extending the resection of the parametrium to the pelvic sidewall, Takayama reported operability rates of 81.5%, including numerous cases of advanced disease [6]. This figure far surpassed the 50% operability achieved by Wertheim [1]. By 1921, Takayama's student Hidekazu Okabayashi had further modified Takayama's approach with the novel technique of separating the posterior leaf of the vesicouterine ligament, which underlies the ureter and connects the posterior bladder and anterior cervix and vagina, allowing for greater development of the perivesical and perirectal spaces which, in turn, allowed for extended vaginal resection, contributing to the increase in operability experienced by these Japanese surgeons [7]. (Author's Note: Of great interest, Dr. Shingo Fujii of Kyoto University has published an article containing links to original videos of Okabayashi performing his radical hysterectomy in 1932 [7].)

The following decades faced waning support for radical surgery for cervical cancer, as newly discovered radiation therapy had moved to the fore in the treatment of many solid malignancies. However, as limitations and long-term morbidity associated with radiation became apparent, attention turned back toward the search for a surgical cure. As such, 1951 became a landmark year in the history of the treatment of cervical cancer.

In his 1951 address to the American Gynecological Society (later published in the American Journal of Obstetrics and Gynecology), Joe Vincent Meigs—an American gynecologic surgeon—presented 100 cases of Stage I and II cervical cancer operated upon with a novel technique: the combination of radical abdominal hysterectomy with Taussig's en bloc pelvic lymph node dissection. Though his radical abdominal hysterectomy was performed in the tradition of Wertheim, Meigs was adamant that his procedure was not simply a “renaissance of the Wertheim hysterectomy” [8].

Meigs noted several deviations in operative technique from that of Wertheim. One such deviation entailed maximally extending the resection of the parametrium and the broad ligament to the pelvic sidewall, similar to Takayama's approach. He recounted that this change came about after a visit by a Dr. C. Kaufmann, who termed the paracervical and paravaginal tissues “Franz Joseph's whiskers” and advocated removing “as much paracervical and paravaginal tissue as the former Emperor of Austria had whiskers.” Meigs commented that this modification was of the utmost importance, citing numerous cases in which lymph channels and nodes containing cancer would have been missed if not for this extended resection. He noted, as well, increased rates of bladder dysfunction associated with this extension of the operation [8].

Similarly, Meigs took notable exception to Wertheim's approach of resecting only those lymph nodes that were enlarged or with palpable findings suggestive of carcinomatous invasion, stating “lymph nodes cannot be determined by inspection, palpation, or visualization and [...] the only proof that lymph nodes are positive or negative is examination in the Pathology Laboratory after their removal.” He thus proposed the addition of Taussig's en bloc pelvic lymph node dissection, stating that “Dr. Taussig showed nodes to me no larger than the head of a match that contained cancer.” [8]. Indeed, in Meigs' experience, 17.5% of patients with Stage I disease and 32.1% of patients with Stage II disease were found to have lymph nodes with carcinomatous foci (particularly obturator and iliac nodes), even in the absence of suspicious features [8].

Meigs likewise noted several other minor deviations from Wertheim's procedure. He did not routinely make use of Wertheim's specially made vaginal clamps, which were designed to impede the spillage of malignant cells into the vagina and the spread of bacteria from an infected carcinoma into the peritoneum. Meigs found that by avoiding clamping the vagina, the attainable cuff size was considerably greater. Similarly, though Wertheim paid careful attention to the curettage and cauterization of the carcinoma, Meigs did not see a need to cauterize or irradiate the tumor prior to operating. Noting that tumor recurrence in the vagina was rare among his cases, Meigs hypothesized that vaginal tumor seeding may not have occurred as frequently as previously thought. Similarly, due to the availability of antibiotics, the spread of infection from a potentially infected tumor focus was not a concern of Meigs' [8].

The results achieved by Meigs with his modification of the Wertheim hysterectomy were astounding. In stark comparison to Wertheim's 18.6% perioperative mortality, Meigs experienced none [8]. The reasons for this disparity are many-fold. Concurring with one of Wertheim's closely held opinions, Meigs advocated for rigorous patient selection, operating only upon patients with favorable risk profiles [1,8]. Likewise, numerous times throughout his address, Meigs noted the prominent role peritonitis played in Wertheim's mortality figures, and credited much of the decrease in perioperative mortality he experienced to the availability of sulfonamide antibiotics. With the addition of routine bilateral pelvic lymphadenectomy and subsequent pathological analysis, Meigs demonstrated that lymphatic invasion was much more common than previously believed, and that en bloc resection of lymphatic tissue afforded greater survival benefit. With these modifications, Meigs achieved an 89.7% 5-year survival rate for Stage I disease, and a 63.0% 5-year survival rate for Stage II disease [8]—far surpassing Wertheim's 18.4% overall five-year survival [1]. Thus, Meigs affixed his

name to the Wertheim hysterectomy, and defined the basis of the current standard of care for the surgical treatment of cervical cancer.

4. Recent trends in the surgical treatment of cervical cancer

4.1. Nerve sparing and lessened radicality

As a testament to the successes of surgical therapy for carcinoma of the cervix, the 1960s hailed an important shift in mentality from a focus on a cure at all costs to a focus on quality of life once a cure was achieved. The first forays into improving post-surgical quality of life were pioneered by the Japanese and focused primarily on improving bladder dysfunction. In 1961, the Japanese surgeon Kobayashi proposed dividing the cardinal ligament into its vascular components superiorly and neural components inferiorly, sparing the nerve bundle upon ligating the vasculature of the cardinal ligament [9]. When the Japanese surgeon Sakamoto first published this technique in the English-language literature in 1988, he reported a 27% increase in patients without post-void residual urine one month after surgery in patients undergoing the nerve-sparing technique [9,10]. In 1998, Maas and Moriya began performing nerve-sparing surgeries consistent with Kobayashi's “Tokyo method” for the first time in the Netherlands. In 2000, the Japanese surgeon Kuwabara proposed further sparing the autonomic nerves in the posterior vesicouterine ligament, and was able to demonstrate a reduction in time to post-void residual less than 50 mL by greater than 12 days in patients undergoing nerve-sparing procedures [11].

As attention further turned toward decreasing post-surgical morbidities, investigation was undertaken as to the degree of radicality needed to achieve optimal disease-free survival. In 1987, the German surgeon Stark raised the question of whether a complete resection of the parametrium was truly necessary for patients with Stage IB cervical cancer, comparing the maximal parametrial resection of the Wertheim-Meigs operation with the limited parametrial resection of the Galvin-Te Linde operation [12]. Metastasis, recurrence, and survival rates were comparable between the two groups, though with markedly higher rates of fistula formation in the Wertheim-Meigs group [12]. Shortly thereafter, in 1991, Photopulos and Zwaag published a study comparing Piver-Rutledge-Smith class II and class III hysterectomies (in which the uterine vessels are ligated medial to the ureter and at their origins from the internal iliac vessels, respectively), in which they demonstrated decreased mean operative time and mean length of stay for those patients undergoing class II hysterectomy as well as comparable rates of fistula formation and recurrence [13,14].

Subsequently, in 1995, Magrina and colleagues published a retrospective analysis examining morbidity and mortality associated with modified radical hysterectomy (with division of the parametria at the medial portion) when compared to standard radical hysterectomy. They found that aggregate complication rates were markedly lower in the modified radical hysterectomy (24%) when compared to the standard radical hysterectomy (70%). Operative mortality was found to be comparable [15]. In 2001, Landoni et al. published a randomized controlled trial with 243 patients, demonstrating that in stage IB-IIA cervical cancer, Piver class II radical hysterectomy was non-inferior to Piver class III in terms of disease recurrence and overall survival, and provided an improved morbidity profile, specifically as measured by mean time to voiding and rates of atonic bladder [14,16].

4.2. Fertility-sparing techniques

In parallel to the advances made in the field of nerve sparing, the idea of fertility sparing emerged from the fact that many women diagnosed with cervical cancer have not yet completed their reproductive years. In 1977, Burghardt and Holzer proposed that microinvasive carcinomas—those with a volume of <500 mm³ and only microscopically visible stromal invasion—were not associated with metastatic spread, and in these limited cases, the uterine fundus need not be sacrificed

[17]. This was the first notion of fertility-sparing treatment in meticulously selected patients with carcinoma limited to the cervix. Nearly 20 years later, this vision came to fruition.

In 1994, the French surgeon Daniel Dargent proposed a landmark procedure in the form of radical vaginal trachelectomy. In his procedure, the cervix, upper vagina, and parametria are resected, leaving the uterine corpus intact. A permanent cerclage is placed, allowing for child-bearing and delivery via cesarean section [18]. Four years later, in 1998, Roy and Plante published the results of their first 30 cases of radical vaginal trachelectomy. Six of six women who attempted pregnancy post-trachelectomy succeeded, resulting in the delivery of four healthy neonates and two ongoing pregnancies at the time of publication. These results touted the successes of a limited resection in patients with stage IA₁ to IIA carcinoma of the cervix [19]. More recently, in 2011, Plante et al. published a case series of 125 women who had undergone radical vaginal trachelectomy with 58 women conceiving 106 total pregnancies. Of these, 73% reached the third trimester and 58% resulted in term deliveries. Most importantly, the oncologic outcome of these cases was not compromised with a five-year disease-free survival rate of 95.8% [20].

With increased interest in minimally invasive approaches in many types of surgery, radical trachelectomy is no different. In 2015, Vieira et al. published a retrospective analysis of outcomes of minimally invasive radical trachelectomy when compared to the open equivalent. They found that, similar to other surgeries performed via laparoscopic approach, blood loss and length of hospital stay were decreased in the minimally invasive cohort, with comparable complication and recurrence rates. Pregnancy rates, however, were significantly higher in the open cohort (51%) when compared to the minimally invasive cohort (28%) [21].

4.3. Minimally invasive and robotic-assisted radical hysterectomy

The notion of performing minimally invasive radical hysterectomy was also proposed by Daniel Dargent. In 1987, Dargent combined the radical vaginal hysterectomy (in the style of Schauta) with a laparoscopic pelvic lymphadenectomy, publishing the first recorded instance of minimally invasive technique used in conjunction with radical hysterectomy [5,9]. Soon thereafter, in 1992, Nezhat published cases of the first laparoscopic radical hysterectomies with pelvic and para-aortic lymph node dissections [22,23]. As the 1990s progressed, the application of laparoscopy in gynecologic surgery continued to gain acceptance. In 1998, Jennings et al. demonstrated similar complication rates, but significantly reduced post-operative length of stay in patients who underwent laparoscopic surgery for gynecologic malignancy when compared to the equivalent open procedures [24].

The turn of the new millennium heralded the advent of the robotic surgical platform. After its approval for general laparoscopic surgery in 2000, da Vinci® surgical technology garnered U.S. Food and Drug Administration (FDA) approval in 2005 for gynecologic surgeries [25]. Shortly thereafter, in 2006, Sert published the first case of robotic-assisted radical hysterectomy (Piver class III), proving that the Wertheim-Meigs operation was feasible without compromising radicality using this platform [26]. In 2008, Fanning et al. published the first case series detailing 20 robotically-assisted radical laparoscopic hysterectomies [27]. In 2012, the Society of Gynecologic Oncology released a consensus statement citing the non-inferiority of robotic-assisted surgery when compared to standard laparoscopic surgery.

In addition to standard laparoscopic and robotic-assisted radical hysterectomy, in 2012, a novel technique known as laparoendoscopic single-site (LESS) radical hysterectomy was reported by Garrett and Boruta [28]. The LESS approach was used to perform a radical hysterectomy and pelvic lymphadenectomy through a 2.5 cm umbilical incision accommodating a port through which four instruments could be passed. Shortly thereafter, in 2014, the first multi-institutional case series of radical hysterectomy with pelvic lymphadenectomy was reported

with a 91% success rate, suggesting that this may be a feasible approach for minimally invasive radical hysterectomy in appropriately selected patients [29]. Benefits of this approach include reduced postoperative pain and improved cosmesis over the standard four-site laparoscopic approach.

5. Conclusions

Remarkable progress has been made in the surgical treatment of cervical cancer in the century following Ernst Wertheim's pioneering operation. Medical advances, including the discovery of antibiotics and the ability to safely transfuse blood paralleled advances in surgical technique, allowing for improved survival. A disease once considered to be uniformly fatal to its bearer, early-stage cervical cancer is now treatable via a number of surgical approaches, including nerve-sparing, fertility-sparing, and minimally invasive procedures designed to improve quality of life. As disease process and patterns of disease spread are further elucidated, focus in the coming years will likely be directed toward identifying patients appropriate for conservative surgical therapy in an effort to further reduce operative morbidity [30], as well as identifying sentinel lymph nodes using indocyanine green dye or near-infrared imaging technology [31].

Conflict of interest statement

None of the authors declare any conflicts of interest.

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