



**UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE
„CAROL DAVILA” din BUCUREȘTI**



2024

**UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE
„CAROL DAVILA”, BUCUREȘTI
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DOMENIUL MEDICINĂ**

**Minimal invasive approach in pelvic non-urolological
malignancies**

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Introduction

Non-urolological pelvic cancers represent a challenge in what concerns not just only the surgical treatment, but also the multimodal oncological one. The complex pelvic anatomy determines a unique evolutive pattern of the malignancy. If for the male patients, the malignant non-urolological pelvic tumors approached in this dissertation are represented mainly by rectal cancer, for women the pathology is more extensive including cervical, endometrial, ovarian, and rectal cancer. We mainly focused on cervical cancer giving the newly emerged controversies in the literature.

Globally, rectal and cervical cancer are an important public health problem, it's incidences being in the top 10 types of cancers with associated high mortality rates (top 5 for cervical cancer and 11 for rectal cancer) [1]. In Europe, Romania is in top 10 countries based on the number of deaths from this pathology in 2021[2]. If in 2011-2021, for cervical cancer the mortality trend was descending, most likely by improving the screening process, for rectal cancer the mortality trend was ascending [2], being considered by some a marker of socio-economic development [3]. This fact has an important impact on the current clinical practice, giving the increased life expectancy and the higher prevalence of colorectal cancer in older patients we deal with a new series of problems in treating them [4, 5].

If in the last decades we witnessed a spectacular evolution of the minimal invasive surgery, including the robotic assisted surgery, in the last years there is a shift of paradigm. Even though the advantages of minimal invasive approach are widely known (smaller incisions with the reduction of parietal wall complications, faster postoperative recovery and superior aesthetic results), the oncological benefits of the minimal invasive radical surgery [6], especially those performed in the pelvis, are now being debated [7, 8].

Also, the last decade brought important modifications to the way we perform the staging and classification of cervical cancer, the role of surgery in the therapeutic management of these patients and moreover, in the type of surgical approach. For the emerging countries which have limited resources a new series of difficulties arose. There are a lot of controversies around the exclusion of the minimal invasive approach from the therapeutic arsenal of cervical cancer treatment after using it for more than two decades. First, we have to assess if surgery still has a role in cervical cancer treatment and if so, can we still use the minimal invasive approach or the risks outweigh the benefits?

Mirroring cervical cancer treatment, the treatment of rectal cancer employs surgery, radiotherapy, and chemotherapy in its management, with the new introduction of targeted treatments (immunoglobulins, monoclonal antibodies, and so on). The success of the surgery depends on the total mesorectal excision with complete circumferential margins. Given the difficult pelvic anatomy, more so by laparoscopic approach, that is constricted by the curvature of the sacrum and the converging tendency of the instruments used, a new type of approach emerged to surpass these difficulties: transanal total mesorectal approach [9]. Even though initially the surgeons were enthusiastic to adopt this new approach, the contradictory information from the literature regarding the oncological benefits made them reluctant. Is transanal approach a new step with curative intent in rectum cancer surgery?

I chose this topic to study given the fact that in Romania the malignant non-urological pathology of the pelvis is an important public health problem with high incidence and mortality. First, given the lack of screening implementation and limited resources we are dealing with difficulties in managing the treatment of these patients. Second, the high complexity of pelvic surgery not only in open surgery, but even more so in minimal invasive surgery brings another set of difficulties. Third, because of the high number of controversies that arose in the literature regarding the surgical management of these patients we need to pay extra attention to this topic, this will not only affect the treatment plan but also the juridical aspects of the medical act.

This thesis has the following objectives:

- To evaluate the role of minimal invasive surgery in the treatment of uterine cervical cancer
- To evaluate the short term postoperative complications after minimal invasive surgery performed for malignant gynecologic pathology.
- To comparatively assess the minimal invasive approach with the open one for colorectal cancer elderly patients
- To evaluate the transanal total mesorectal excision comparatively with the other minimal invasive techniques

The role of minimal invasive surgery in uterine cervical cancer treatment

Introduction Until recently, surgery represented the cornerstone in treating advanced loco-regional cervical cancer. In the last decade, radiotherapy and chemotherapy have made important advancements improving the long term survival of these patients and lowering the recurrence rate. Considering the evidence provided so far, many cancer treatment centers recommend a treatment based solely on chemo-radiotherapy and exclude surgery. In Romania, surgery is one of the main steps in treating cervical cancer patients. The current data shows that a large number of these patients are still being sent to surgery regardless of the clinical stage. Establishing the role of surgery in the treatment of advanced loco-regional cervical cancer is of utmost importance for the surgeon, but also for the radiotherapist, in their efforts to provide the best survival.

Oncological surgery is constantly evolving, the recommendations and the guidelines are periodically updated in the light of the new evidence. In the last five years, the minimal invasive surgery used in gynecology took a considerable advance, considering that the complication rate and the postoperative recovery markedly decreased [10]. Because surgery is an important step in the treatment of cervical cancer in Romania and considering the new studies, we want to thoroughly assess the updates in the surgical treatment and the new guidelines. We presented a series of cases using protective surgical techniques to avoid tumor dissemination during minimal invasive surgery. Also, we want to assess the cervical cancer specific mortality rate in European Union and Romania.

Material and method In order to achieve the first objective we performed an advanced search of PubMed database, in the last 5 years (from 2018 to 2023), using as filter English language and the following key terms: “ uterine cervical cancer” and “ minimal invasive surgery” or derivative terms (as “laparoscopy”, “robotic” and so on). We did a narrative literature review to underline the changes in the treatment of uterine cervical cancer.

Second, we searched the database of Fundeni Clinical Institute, General Surgery department between 2018 to 2023 to identify the patients with uterine cervical cancer in which intraoperatively a vaginal cuff was performed and also a total mesometrial excision. The identified cases were presented.

Third, we used the EUROSTAT [2] database to select the variables of interest for 27 countries members of European Union, for a 10 year period 2011 to 2020.

Results

Narrative literature review Until now the guidelines accepted also the minimal invasive approach as a valid option in cervical cancer surgery, to perform the radical hysterectomy in stage IA2 to IIA cervical cancer [11].

In 2018, Ramirez *et al* [11] conducted a prospective multicenter randomized trial to properly evaluate the survival outcomes after minimal invasive surgery or OS in early-stage cervical cancer. The results would lead to a major paradigm shift in cervical cancer surgery. The enrollment of patients was early closed by the data and safety monitoring committee because minimal invasive surgery was linked with higher rates of death [11]. evaluated at 4.5 years, the rate of disease-free survival was 86% for minimal invasive surgery and 96.5% for OS [11].

In addition, Melamed *et al* [12] conducted an epidemiological study that would indisputably link the minimal invasive surgery to shorter survival rates than open surgery for IA2 and IB1 cervical cancer patients. The adoption of minimal invasive surgery coincided with a decline in the 4-year relative survival rate of 0.8% per year after 2006 [12].

As with other major paradigm shifts in the medical field, debates emerged. One of the controversies is surgical proficiency. Vergote *et al* [13] acknowledged that the surgical proficiency should be considered the most important issue of a surgical trial pointing out that in the LACC trial some of the participating surgeons had not completed a fellowship in gynecologic oncology and some were general surgeon with surgical oncology fellowships, and most had not published their results in minimal invasive surgery hysterectomies. The measurements of the length of parametria as a parameter of the radicality, was not performed [13].

Another argument as identified by Kimming *et al* [14] was that the minimal invasive surgery arm recruited an average of only 2 patients per center per year raising the question if all surgeons had the chance to maintain sufficient experience during the decade of accrual. Another argument was that the choice of type II or type III minimal invasive surgery radical surgery was left to the operating surgeon. There were no protocol guidelines indicating which type of surgery should be performed for which size [13].

Other controversy started from the fact that the control group, open surgery approach, performed unexpectedly well, with a low result for recurrences [14, 15]. Given the fact that histological data on tumor size was missing in a third of open surgery cases, this may be due to the incomplete data presented [14]. Another perspective is the characteristics of the cohort.

The scientific community attempted to understand the causes why minimal invasive surgery does not provide a similar oncological outcome as open surgery. Taking into

consideration the basic principles of oncologic surgery, the following weak points were identified as possible causes. The surgical technique of minimal invasive surgery radical hysterectomy is associated with the use of uterine manipulators [16, 17]. This can condition the spread due to erosion and friction of the tumor, even leading to its perforation [18]. Another possible cause was that tumor cells may spread within the peritoneal cavity by circulating carbon dioxide when intra-peritoneal colpotomy is performed above the manipulators rim [16-18].

Other possible reason may be the experience of the surgeon, the learning curve, if he has the experience to perform oncological gynecologic minimal invasive surgery [19].

In 2020, the SUCCOR study revealed similar results: minimal invasive surgery is associate with increased risk of relapse and death compared to open surgery [20]. Additionally, this study determined that by non-using the uterine manipulator and adopting maneuvers to avoid tumor spread during colpotomy (protective vaginal closure), the minimal invasive surgery patients had similar outcomes as those with open surgery[20]. Protective operating techniques result in improved survival [21].

To address this issue, Köhler *et al* [16] established a surgical technique that combined the minimal invasive surgery and vaginal approach: laparoscopic radical hysterectomy with transvaginal closure of vaginal cuff.

Multiple surgical techniques were proposed, but they can be grouped as follows: transvaginal approach or intracorporeal approach. For the transvaginal approach, the surgeon creates the vaginal cuff with a purse string suture after approximating the margins with straight Kocher clamps [16] or with simple interrupted stitches reinforced by a purse string [22]. Some authors propose to first incise circumferentially the vaginal mucosa and after that the cuff is closed with a running suture [18]. The intracorporeal approach implies that the vagina should be clamped with a bulldog or sectioned using a surgical stapler [22]. The vaginal cuff length is not associated with the local recurrence [23].

In 2003, Höckel *et al* [24] proposes the total mesometrial resection (TMR) based on developmentally defined surgical anatomy inspired by the advances made in the surgical treatment of rectal cancer: the introduction of total mesorectal excision based on the same principle. This technique was soon translated to robotic surgery with similar results [25].

Case series presentations Considering the surgical techniques prior presented we show that the vaginal cuff closure and the total mesometrial excision can be safely used at the same time improving the prognostic of cervical cancer patients that had undergone minimal invasive surgery.

Cervical cancer specific mortality rate in European Union and Romania

Initially we evaluated the life expectancy for women at birth in the last 10 years in European Union. It registered a statistically significant increase ($p=0.0037$) of 0.4 years. The mean in European Union is around 82-83 years during the survey period, with a sharp decrease in 2020. In Romania, the life expectancy of women is around 78-79 years, well below the European mean, even though until 2019 it registered a positive trend. This may be due to the COVID-19 pandemic[26].

In what concerns the cervical cancer screening, the trend in European Union is situated between 48% and 56% during 2011-2020. The smallest percentage of screening registered is of course in 2020. The data reported by Romania is situated well below the European mean, the top percentage is of only 8% registered in 2014.

The mean number of women diagnosed with malignant tumor of the uterus reported for 100 000 inhabitants was relatively constant in European Union with an annual average ranging from 68.7 and 80.4 per 100 000 inhabitants, but comparatively Romania reported a range of 101.6 to 177.5 per 100 000 inhabitants. Taking into account that this range of pathologies include also the cervical cancer, most likely the reported data by Romania is increased because of it considering that Romania is ranked 3 in European Union in the incidence of cervical cancer.

The mean number of reported hysterectomies per 100 000 inhabitants registered a marked decrease in the investigated period in the European Union, most likely by limiting the surgical indication. But even though this trend has a downward tendency, the mean number of laparoscopic hysterectomies was progressively increasing until 2019 when given the start of COVID-19 pandemic the wide scale utilization of minimal invasive approach was halted due to sanitary motives, there was a high suspicion of virus aerosolization and accelerate transmission. In Romania, not considering the data from 2019, the trend of the number of hysterectomies was relatively constant with a progressive gain of the cases performed by minimal invasive approach.

The cervical cancer specific mortality rate reported per 100 000 inhabitants has a downward tendency in European Union with a statistically significant difference between the median from 2011 of 2.8 and that of 2020 of 2.5 per 100 000 inhabitants ($p= 0.005$). In Romania the reported values are almost three times higher than the reported European mean even though a constant downward trend was registered in the period 2011-2020, from 8.2 to 7 per 100 000 inhabitants.

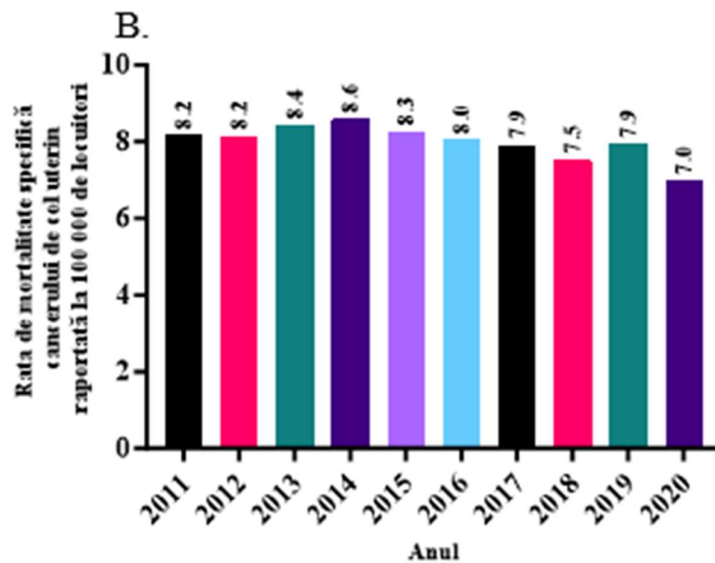
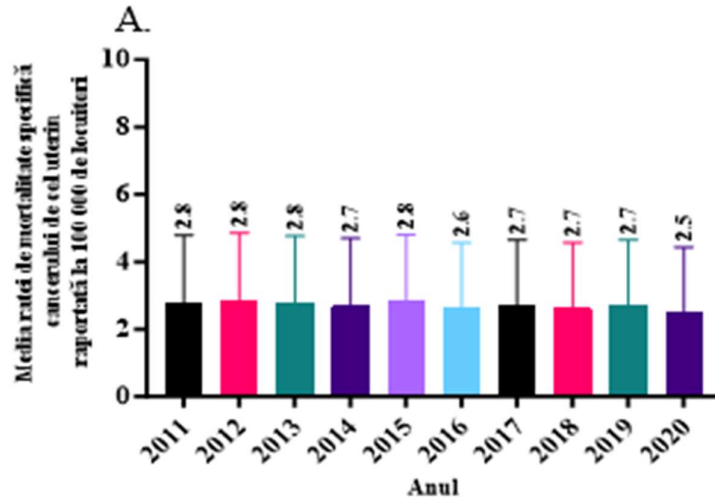


Figure 1 A. Average cervical cancer specific mortality rate reported per 100 000 inhabitants in European Union between 2011 to 2020

B. Cervical cancer specific mortality rate per 100 000 in Romania between 2011 to 2020

Conclusion The paradigm shift in minimal invasive approach for cervical cancer that took place in 2018 brought up the question: is there still a role of minimal invasive surgery in the treatment of cervical cancer? Köhler surgical technique seems to address some of the issues raised by the minimal invasive surgery with good results. Höckel proposes total mesometrial excision to decrease the risk of recurrence. The case series presented showed that is feasible and safe to merge these techniques. Also, by analyzing the data reported in European Union and in Romania we identified a considerable increased difference in the

cervical cancer specific mortality rates reported by the last one. Further prospective studies are needed in order to assess the risk and benefits of these techniques.

Postoperative complications after minimal invasive surgery for gynecologic malignancy

Introduction In recent years, minimal invasive surgery for gynecologic pathology has become the preferred option for many gynecological disorders [27] since complication rate and postoperative recovery time have decreased considerably [10]. Intraoperative and postoperative complications associated with minimal invasive surgery are a serious problem if inadequate diagnosis and treatment, particularly for the urological ones. They (vesico-vaginal, vesical or ureteral fistulas and ureteral stenoses) can lead to long-term complications such as varying degrees of hydronephrosis or renal failure [28], remaining the basic problem in gynecological minimal invasive surgery, both clinical and medico-legal [28].

The main aim of the study is to assess the incidence of the postoperative complications occurring in minimal invasive surgery for gynecological malignancies and their specific management, emphasizing the urological ones. The second purpose is to perform an assessment of possible risk factors on pre- and intra-operative variables and to evaluate the impact of the type of minimal invasive surgery used.

Material and methods The retrospective cohort study used the database of the General Surgery Department, searching between 2008 and 2019 for patients with gynecologic pathology. 2907 cases were acquired. An additional selection was performed using the following filters: minimal invasive surgery and neoplasia. All emergency surgeries were excluded. 198 cases were obtained.

Results The mean age was 53 years old with a minimum of 23 and a maximum of 78 years old. The mean postoperative hospital stay was of 7.58 days with a minimum of 3 days and a maximum of 64 days. Regarding the operative time, the mean was 240 minutes with a minimum of 80 minutes and a maximum of 570 minutes. Most of the patients had an ASA score of 2, 58.6% (n=116). 34.8% had ASA 3 and a number of thirteen patients had ASA 4 representing 6.6%.

In what concerns the comorbidities, the majority of the patients, 33.3% associated cardiac pathology, in 13.6% obesity and in 8.6% autoimmune disease.

Figure 2 presents the distribution of the patients by tumor location. The conversion rate was 3.5% and in just 2% of cases an exploratory laparoscopy was performed. The type of minimal invasive approach predominantly used was the robotic one, 68.2%.

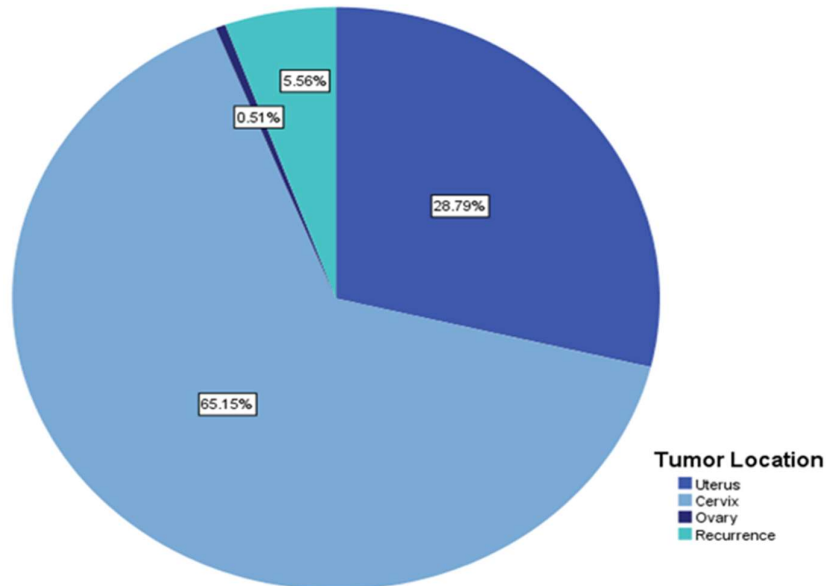


Figure 2. The distribution of the cases by tumor location in percentages

Most of the patients, 151 (76.3%), had a Piver III hysterectomy. Twenty patients, 10.1%, had a Piver II hysterectomy. 5.1% of the patients, 10 cases, associated other resections to the Piver III hysterectomy and the same number of patients with anterior pelvic exenteration. For total pelvic exenteration 3 cases, 1.5%, were registered and a similar percentage for the resection of the local recurrence. Only one patient had a posterior pelvic exenteration (0.5%).

85.4% of the surgeries were performed by a surgeon with experience both in minimal invasive surgery and proficient in gynecological surgery. The rest of the cases, 14.6% were performed by surgeons with extensive experience in minimal invasive surgery, but basic training in gynecologic surgery.

The Dindo-Clavien classification was used in order to reduce the biases when reporting the postoperative complications. 76.3% of cases had no complications. In 2.02% cases, the study reports grade I complications and in 13.13%, 26 cases, grade II. Eleven cases, 5.56%, had grade IIIA complications and 3.03%, 6 cases, had IIIB complications. Detailed assessment of the postoperative complications are depicted in Table 2. The majority of the complications were urological, 11.6% from which 7.07% required specific urological procedures. Only in 1.51% of cases a surgical procedure was needed, the most frequent

procedure was insertion of double-J catheter 3.03%, followed by urethrovessical catheterization 2.02% and 0.5% nephrostomy.

In order to assess a possible correlation between the Dindo-Clavien Classification and the other variables, the Spearman's Rho coefficient was employed. Dindo-Clavien classification correlates positively with the PHS ($p=0.000$), the type of surgery ($p=0.046$), the primary tumor location ($p=0.011$), conversion ($p=0.049$), the surgeon ($p=0.012$) and the operative time ($p=0.002$).

Primary tumor locations correlates positively with postoperative hemorrhage ($p=0.026$), pelvic abscess ($p=0.015$), venous thrombosis ($p=0.001$) and cardiac complications ($p=0.015$).

The type of surgery correlates positively with postoperative hemorrhage ($p=0.017$) and venous thrombosis ($p=0.002$). The operative time correlates positively with wound and parietal complications ($p=0.025$), pelvic abscess ($p=0.027$) and venous thrombosis ($p=0.013$). The conversion correlates positively with the presence of wound and parietal complications ($p=0.000$), postoperative hemorrhage ($p=0.046$) and venous thrombosis ($p=0.020$).

In order to evaluate the differences between the type of minimal invasive approach, the cohort was divided into the robotic group (RG) and the laparoscopic one (LG). The patients in the RG had a mean postoperative hospital stay of 8.38 days, as opposed to those in the LG of only 5.89 days ($p=0.025$). The comparative assessment of the primary tumor location distribution in the groups is depicted in figure 3, being statistically significant different ($p=0.011$). There were no statistical differences between the groups in what concerns the postoperative complications ($p=0.606$), even though the type of surgery was different ($p=0.000$) with more complex surgeries allotted to the robotic group.

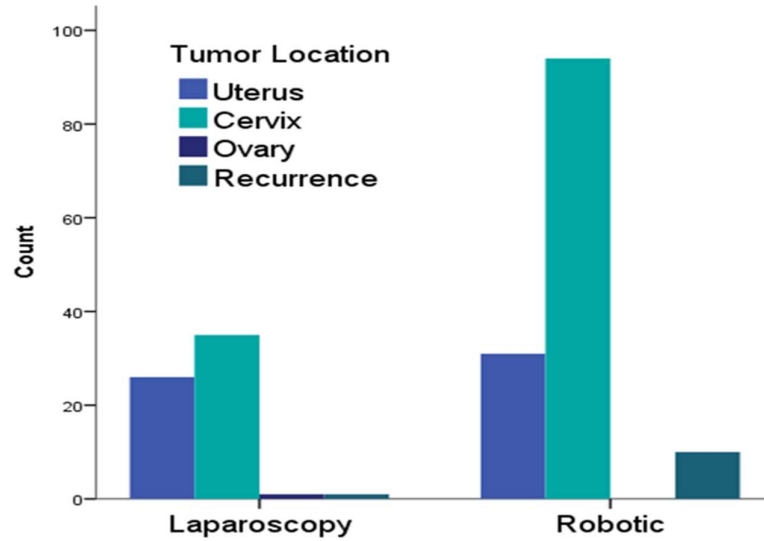


Figure 3. The comparative assessment of the primary tumor location between the laparoscopic and robotic group

Conclusion Minimal invasive surgery is a safe alternative for gynecological malignancies in terms of postoperative complications. Urological complications remain an important problem in oncologic gynecologic surgery and needs to be diagnosed and addressed rapidly. Another important complication identified was lymphorrhea, even though some studies report lower rates after minimal invasive surgery. The robotic approach is able to perform more complex surgeries, including recurrences, with no difference in the postoperative complication rates. Another important aspect is the extensive experience of the surgeon in gynecologic surgery that correlates with reduced postoperative complications. Further prospective studies are needed to confirm the superiority of one approach over the other.

Comparative analysis of minimal invasive versus open approach for colorectal cancer elderly patients

Introduction Currently, surgeons deal with an older patient cohort and therefore, are confronting with new challenges. The life expectancy has raised and so the incidence of neoplastic disease, especially that of colorectal cancer (CCR) [29]. Approximately 70% of the newly diagnosed colon cancers occur in patients older than 65 years, CRC being an age-associated malignancy [4]. Compared with their younger counterparts (35-69 years old),

patients older than 70 years receive 50% less treatment [30]. They are unrepresented in surgical clinical trials [30, 31], the vast majority of studies being observational, and so there is a lack of data in regard with the optimal surgical treatment of this age group [32].

Surgery is considered challenging for this patient group due to their frailty caused by reduced physiological reserves and frequent comorbidities[33]. Comparing OS versus MIS in CRC over an age limit would lead to new evidence regarding the surgical therapy of choice for this group. Significant controversy remains when it comes to MIS in the elderly as some studies report increased risk of complications, whereas others consider it safe[34]. The question that future guidelines need to address is if MIS is a safe approach for CRC elderly patients.

The main goal of this study is to evaluate the characteristics and the differences in the short term outcome after MIS and OS approach in CRC elderly patients, defined as individuals of 65 years old or older. The secondary goal is to identify preoperative risk factors for postoperative complications.

Material and methods The study is a retrospective propensity score match case-control. Initially, the database from the General Surgery Department was inquired between 2012 and 2015 for patients older than 65 years with malignant colorectal pathology undergoing elective surgery using the following filters: age ≥ 65 and diagnosis of rectal or colonic adenocarcinoma. Propensity score match case-control was used to limit selection biases, to compare the results with a control group that had undergone OS for the same tumor location, stage, and type of surgery (radical or palliative), with the same age and gender of the patient. Figure 4 depicts the selection process.

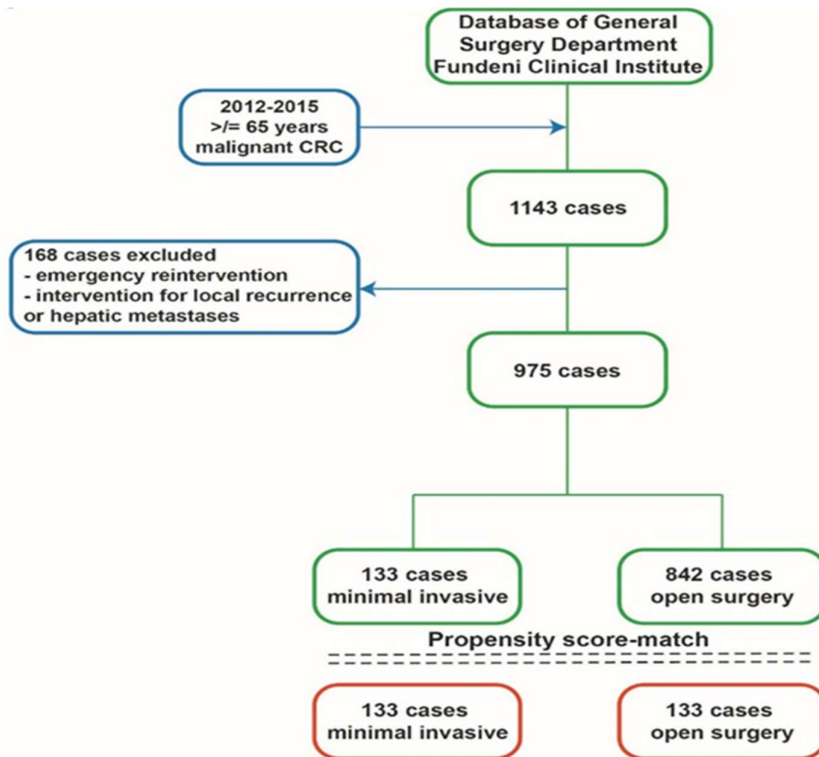


Figure 4. Flowchart illustrating the selection process

Results After analyzing the entire cohort prior to matching, the mean age was 73 years old with 60% of the patients being males. In what concerns the primary tumor location the majority 28% were located on the right colon, followed by the left colon 27%, superior rectum and rectosigmoid junction 25%, lower rectum and anal canal 16% and in 4% of cases there were synchronous tumors. Regarding the tumor stage, 3% were stage 0, 15% stage I, 38% stage II, 25% stage III and 19% stage IV.

Eighty-six percent of the surgeries in this cohort was performed by an open approach. From 14% of the MIS approach 73% were laparoscopic (97 patients) and 27% robotic (36 patients). We recorded a conversion rate of 7.52% (10 cases), these patients were included in the open surgery group due to the greater surgical trauma. In 18% of cases, the type of surgery was palliative.

After performing the match using gender, primary tumor location, the type of surgery, tumor stage and age the preoperative variables showed a statistically significant difference in what concerns the presence of chronic pulmonary disease ($p=0.039$), with more cases allotted to the open surgery group, 14%.

Regarding intra- and postoperative variables, we observed that there are statistically significant differences between the groups in what concerns the type of anastomosis: more

stomas and more manual anastomosis in the open surgery group and more mechanical anastomosis in the minimal invasive surgery group ($p = <0.001$). As well, for the protective stoma variable there were more cases for which this did not applied either because it was a terminal stoma or because it was a right hemicolectomy in which a protective ostomy has no role ($p = 0.024$). Even though there were no statistically significant differences between the groups in regard with postoperative complications ($p = 0.699$), the days from surgery to discharge were statistically significant different with a shorter stay for the patients in minimal invasive surgery group ($p = 0.025$).

In order to investigate the effect of the statistically significant preoperative variables on the matched group and to assess if they are risk factors for postoperative complications a group subanalysis was performed.

We observed that chronic lung disease and Clavien-Dindo classification are significantly associated (Chi-square test, $p < 0.001$). There is a significant difference (t-test, $p = 0.028$) in the number of days from surgery to discharge between the patients with chronic lung disease (mean number of days is 16) and those without chronic lung disease (mean number of days is 11).

Thirty-six patients from the matched cohort had uncontrolled diabetes (15 from the open surgery group and 21 from minimal invasive surgery group). There is no significant association between the presence of uncontrolled diabetes and the surgical approach (Chi-square test, $p = 0.282$). When analyzing the entire cohort, this variable did not reach a statistically significant association neither with Clavien-Dindo classification (Chi-square test, $p = 0.120$) nor with days from surgery to discharge (T-test, $p = 0.337$).

Conclusion The elderly are a heterogeneous population, and the chronological age alone should not be a limit to MIS, granting the fact that it is effective and safe for CRC patients. The minimally invasive approach showed no inferiority to the open approach in terms of postoperative morbidity, correlating with lower postoperative stay in the elderly. Chronic lung disease is associated with postoperative complications and postoperative hospital stay. Further prospective studies are needed to assess the outcome of MIS in the elderly population.

Minimal invasive surgery for rectal cancer: TaTME, Robotic or Laparoscopic approach?

Introduction Transanal total mesorectal excision (TaTME) is a relatively new surgical technique which quickly became an alternative in rectal cancer surgery. Introduced for the first time in 2010 [35], it was obvious that renders great benefits in surpassing the technic and anatomical difficulties of laparoscopy.

The controversies regarding this method arose in July 2019 when Norway emitted a moratorium on this technique motivated by the high local recurrence rates registered (9.5%), that would be held until the national audit results [36]. This raised a lot of questions [37-39], many of them referring to the previous experience of the surgeons in laparoscopy and transanal endoscopic training, learning curve, the low number of cases per center, the neoadjuvant therapy or the intraoperative complications reported, as perforation or the failure of the string purse performed inferior to the tumor.

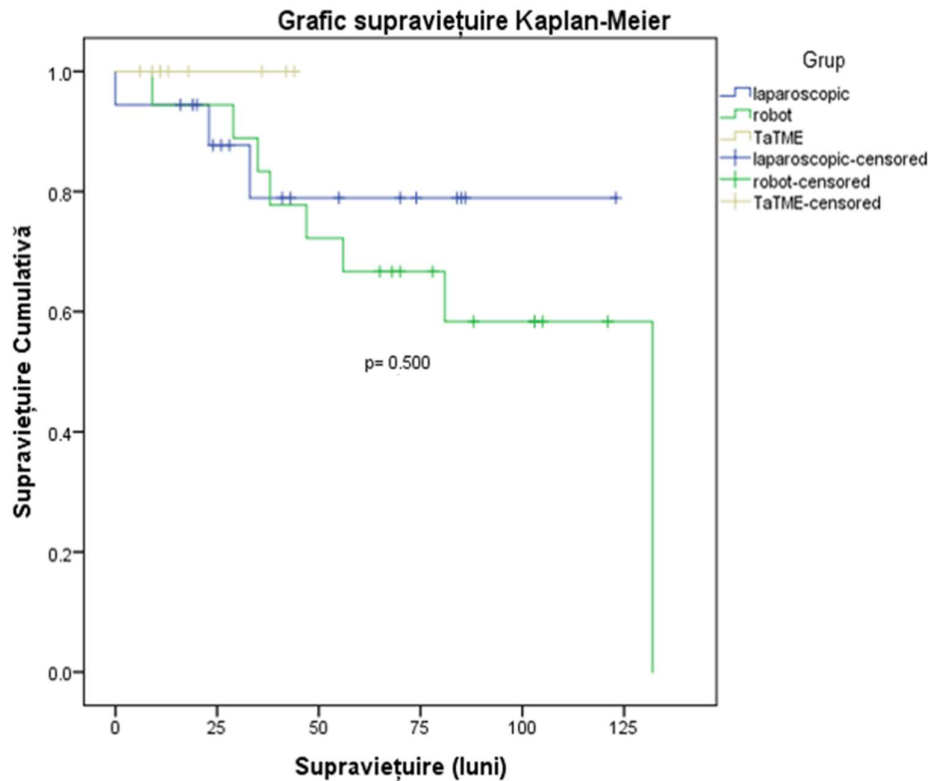
The present study analyses the differences between TaTME, LaTME (laparoscopic total mesorectal excision) and RTME (robotic total mesorectal excision) in what concerns the preoperative variables, postoperative outcome and overall survival.

Material and methods This is an observational, longitudinal retrospective study match case-control. We selected the cases with rectal adenocarcinoma stage I to IIIC in which a total mesorectal excision was performed by minimal invasive approach (TaTME, LaTME or RTME) between 2008-2022, in General Surgery Department of Fundeni Clinical Institute. We excluded the cases that had invasion of the sphincteric apparatus, emergency surgeries and surgery for local recurrence.

After using the above criteria, we obtained 3867 cases. To limit the selection bias and the bias given by the sample size we performed match case control analysis 1:2 (TaTME 1: LaTME 2: RTME 2). The variables used for the match were the following: stage, primary tumor location, type of surgery, age (± 2 ani) and gender. The 45 cases selected were divided in the 3 groups.

Results The first case of TaTME was performed in 2019 in Romania [40]. The only statistically significant difference in the preoperative variables was the ASA score ($p=0.026$), with more cases of ASA III in the LaTME and RTME group. The operative time was the only statistically significant different variable from the intra- and post-operative variables ($p=0.000$), with a considerably higher operative time for TaTME. To underline the

differences in the overall survival we used the Kaplan-Meier graph and the log-rank test to assess if there is a statistically significant difference, as represented in figure 5. Even though we can see a difference in trends there is no significant difference.



Număr decese	1 an	3 ani	5 ani
TaTME	0	0	0
LaTME	1	3	3
RTME	1	3	6

Figure 5. Comparative assessment of the overall survival

Conclusion TaTME is a relatively new surgical approach in the treatment of rectal cancer that offers multiple advantages. A careful selection of the patients and the extensive experience of the surgical team in minimal invasive surgery are the basis of a better implementing of the technique. The short term postoperative results are similar between the groups, the only difference is in what concerns the operative time, much higher in the transanal group. The learning curve and the implementation of the technique in new centers which respect the general recommendations should render similar results to the literature. In what concerns the overall survival we should state that this technique is not inferior to the others, but further prospective studies are needed to confirm the oncological benefits of the method.

Conclusion and personal contributions

The malignant pathology of the pelvis, specifically cervical and rectal cancer, have high incidence and mortality worldwide, but more so in Romania. They are important health problems. If for cervical cancer, the primary preventive measures, vaccination, could drastically reduce the incidence, this method is not widely accepted by the population and the percent of HPV vaccinated women in Romania remains low that translates into a high incidence of the disease : Romania is on the third place in Europe. Another approach could be implementing national screening programs, both for cervical but also for rectal cancer, but the percent of people that did not underwent any screening for both pathologies are high: in 2019, Romania is on first place with 47.4% of the population that did not perform a screening test for cervical cancer and on third with 93.1% of the population that did not performed any screening test for colorectal cancer. For rectal cancer, starting with 2020, a national screening programme was developed: ROCCAS.

The surgical management of these pathologies poses high difficulty. First, from an anatomical point of view, the pelvis is a narrow space, that contains a series of organs and anatomical structures that can be accidentally injured intraoperatively given the proximity and the curvature of the sacrum increases the difficulty of the dissection, the surgeon needs to master the spatial disposition of the anatomy. Given the lack of parietal peritoneum, the malignant pathology of the pelvis has an unique evolutive pattern, with a predilection for loco-regional invasion, that permits in advanced T stages to perform extensive curative resections when there are no distant metastasis and the disease it's confined to the center of the pelvis. Moreover, this makes feasible the use of external radiotherapy, but also for brachytherapy with superior results, going further in some pathologies as to exclude the surgery from the treatment plan.

Pelvic minimal invasive surgery has succeeded in offering a better visualization of the anatomy, but it came with a series of limitations, more so for the laparoscopic approach. The pelvic geometry determines the instruments used in laparoscopy to converge for the structures situated more profound situated, rectal surgery being the mainly affected. The surgical specimen after total mesorectal excision is supposed to be cylindrical in shape, with complete circumferential margins, but in laparoscopy this is difficult to achieve, the surgical specimen can vary and be conical, an important thing to avoid. Robotic surgery brings new technological advantages to overcome this: 3D vision, articulated instruments that can perform 360° movements and the possibility to coordinate more surgical arms by the leading

surgeon. Considering the numerous benefits for the patient, but also for the surgeon, it was widely adopted. Minimally invasive surgery rapidly became the method of choice in the treatment of a lot of diseases and also is widely used in oncological setting. In the last decade, in the surgical oncology the use of minimally invasive approach started to be questioned. It is necessary to validate the non-inferiority of this approach to open surgery for the long term oncological aspects. Even though we are tempted to consider that no matter the type of approach the surgical intervention is the same, the alarm came in 2018 when a prospective multicenter randomized study showed that minimal invasive approach for cervical cancer comes with higher recurrence rates and lower overall survival compared with open surgery [11]. The right way to validate a new surgical technique can be difficult, this was also registered for the transanal total mesorectal approach in rectal cancer (TaTME). Even though the technique was developed in order to overcome some of the anatomical difficulties for the low and medium rectal cancer and to avoid the incomplete specimens sometimes found in laparoscopy, the wide adoption of the technique was hampered by the conflictual data published: in 2019, Norway emitted a moratorium on this technique until the national audit data will be available [36]. The national audit showed higher recurrence rates, multifocal or extensive recurrence and a higher percentage of anastomotic leaks that mandated the halt of using this method. After that a lot of controversies appeared.

One of the objectives of this thesis was to address the difficulties in the minimally invasive surgery of the malignant non-urological pathology of the pelvis and the controversies arose in the literature. Following the above mentioned objectives, we will first address the role of minimal invasive surgery in the management of uterine cervical cancer. Even though the role of surgery in the treatment of the cervical cancer is a limited one, the current clinical practice in Romania differs from the international guidelines because of the limited resources and the difficult access to radiotherapy [41]. From 2018, the minimal invasive approach was eliminated from the international guidelines. After performing a narrative literature review and assessing the controversies in the literature, we identified new modalities that could remedy the so considered weak point of the minimal invasive approach for this pathology. Combining a series of surgical gestures with oncological surgical principals: performing a vaginal cuff closure that would seal the tumor with the colpotomy being done transvaginal the risk of tumor spillage will be reduced and also by performing the Höckel total mesorectal technique, we showed by presenting a series of cases that is feasible and safe to be merged. Furthermore by using the EUROSTAT[2] database, we identified a major difference between the data reported by European Union and that of Romania in what

concerns the specific mortality rate. Further prospective randomized studies on large cohorts are needed to assess the oncological safety of this method.

Next, we evaluated the postoperative morbidity and mortality of minimal invasive approach for gynecologic malignancies. The postoperative complications remain a critical subject of this approach, especially for malignant pathology, and they need to be promptly identified and addressed quickly, if possible intraoperatively, or immediately postoperative and treated immediately [43]. By assessing the General Surgery Department, Fundeni Clinical Institute database, we demonstrated similar results with those reported in the literature for open surgery. Minimal invasive approach is similar to the open one in what concerns the postoperative complications. Also, we identified the urological complications as being the more predominant and we described the specific management. The robotic approach seems to render great advantages in this pathology because more complex surgeries were performed in this group with similar postoperative complication rates as in the laparoscopic group. As risk factors for postoperative complications we identified that a major impact has the experience of the surgeon in gynecologic surgery and is correlated negatively with the complication rate.

Colorectal cancer is frequently treated as a unique pathology in the literature even though the therapeutic management is different and nowadays is clearer that this are two distinct pathologies with different risk factors. The incidence of this pathology is rising with the age. Globally the life expectancy has raised and with it the incidence of malignant pathologies, especially that of colorectal cancer. This determined that the surgeon has a new set of unique problems that appeared by dealing with elderly[5]. We tried to determine the role of minimal invasive surgery in elderly colorectal cancer patients and in order to minimize the bias of selection and to offer this retrospective study the characteristics of an experimental design we used the match case-control technique by utilizing the propensity score. Even though the elderly population is heterogeneous, the chronological age should not be an impediment for minimal invasive surgery given the fact that is efficient and not inferior to open surgery: not from the postoperative morbidity, with a shorter postoperative hospital stay that for the elder patient may render additional benefits. In this cohort the patients associated chronic pulmonary disease that was positively correlated with the postoperative complication rate and longer postoperative hospital stay.

The ongoing technological development and the need to surpass the difficulties given by the pelvic anatomy, made possible the development of a new approach for rectal cancer: transanal total mesorectal excision. TaTME showed a lot of advantages over the other

approaches, but the controversies in the literature halted its widely adoption. The first case of TaTME performed in Romania was in 2019[40]. We comparatively assessed the three minimal invasive approaches: laparoscopic, robotic and transanal and to avoid the selection bias we performed match case-control. We did not registered any differences in what regards the conversion rate, reinterventions, anastomotic leakage, positive distal margins, morbidity, mortality and the number of harvested lymph nodes. The only difference was of the operative time with higher values for TaTME. The learning curve and implementation of the method in new centers needs to respect the guidelines to render similar results to those shown in the literature. The overall survival did not differ between the groups. Further prospective studies are needed to assess the oncological benefit of the method.

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