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The role of exenterations in the treatment of advanced pelvic cancers – current concepts
SUMMARY OF THE DOCTORAL THESIS

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Table of Content

Table of Content **I**

List of published scientific papers **IV**

List of abbreviations and symbols **VI**

INTRODUCTION **1**

I. Generalities **8**

1. Surgical technique of exenterations **8**

1.1. Classification of pelvic exenterations 8

1.2. Description of the surgical technique 8

1.2.1. Anterior hemipelvectomy technique 8

1.2.2. Posterior hemipelvectomy technique 11

1.2.3. Total pelvectomy technique 13

1.3. Surgical techniques auxiliary to exenterations 13

1.3.1. Genitourinary reconstruction 14

1.3.2. Digestive reconstruction 16

1.3.3. Pelvic floor resection and soft tissue reconstruction 16

1.3.4. Resection and reconstruction of vascular axes/nerve structures 17

1.3.5. Resection and reconstruction of the bone pelvis 18

2. Role and results of pelvic exenterations in neoplastic diseases **20**

2.1. Indications 20

2.1.1. Curative/Radical 20

2.1.2. Paliative 20

2.1.3. Part of the multimodal therapeutic concept "To Gain Time" 21

2.1.4. Laparoscopy/Robotic Surgery 21

2.2. Contraindications and limitations 22

2.2.1. Tumor biology 22

2.2.2. Surgical Aspect 24

2.2.3. Patient characteristics 25

2.3. Morbidity and mortality associated with pelvectomy 26

2.4. Oncological results of pelvectomy 27

2.4.1. Overall survival in gynecological cancers: 32

2.4.2. Survival without signs of disease in gynecological cancers 32
2.4.3. Overall survival in colorectal cancers 32
2.4.4. Survival without signs of disease in colorectal cancers 33
II. Personal contributions 34
3. Working hypothesis and general objectives 34
4. General research methodology 36
5. Study 1 – Pelvectomies at IOB (Preliminary Experience) 39
5.1. Introduction 39
5.2. Materials and method 40
5.3. Results 42
5.4. Discussions 48
5.5. Conclusions 50
6. Study 2 – Analysis of Socio-Demographic Factors Influencing the Need for Pelvic Exenteration 51
6.1. Introduction 51
6.2. Materials and method 52
6.3. Results 53
6.4. Discussions 60
6.5. Conclusions 73
7. Study 3 – Pelvic Exenterations: Which Patients Are They Intended For, and What Outcomes Do They Achieve? 74
7.1. Introduction 74
7.2. Materials and method 74
7.3. Results and discussions 75
7.4. Conclusions 91
8. Study 4 – Quality of Life of Patients After Pelvic Exenteration 92
8.1. Introduction 92
8.2. Materials and method 93
8.3. Results 94
8.4. Discussions 101
8.5. Conclusions 112
9. Study 5 – Developing a Clinical Guide for Selecting Patients in Order to Achieve an Optimal Risk–Benefit Ratio for Pelvic Exenteration 113
9.1. Introduction 113

9.2. Materials and method 113
9.3. Results and discussions 115
9.4. Conclusions 121
10. Conclusions and personal contributions 123
Bibliography 126
Annexes 160

With a history of more than 80 years, pelvic exenteration (pelvectomy), defined as the complete or partial resection of the pelvic viscera and the lymphatic drainage systems associated with the excised organs, is a surgical procedure that has evolved constantly over time, undergoing changes in technique as well as in concept (improvement of the surgical approach, shift of the intervention spectrum from palliative to radical, modification of indications and contraindications). It therefore remains a subject of ongoing interest and continues to hold its place within the arsenal of oncologic surgery.

The motivation for choosing the topic "The Role of Exenterations in the Treatment of Advanced Pelvic Cancers – Current Concepts" becomes evident in the context outlined above.

The importance and relevance of this topic lie in the fact that, despite the morbidity and quality-of-life implications it entails, pelvic exenteration remains the only therapeutic option capable of achieving long-term survival. It is indicated as primary or "salvage" therapy for selected cases of locally advanced pelvic malignancies that have not metastasized beyond the anatomical boundaries of surgical resection. This is readily apparent to the clinician with extensive experience in oncologic surgery. Nevertheless, there is no international consensus regarding the role of these highly invasive, mutilating procedures in the treatment of neoplastic diseases. The variability in such opinions may stem from the fact that existing studies used different enrollment criteria, examined heterogeneous patient populations and tumors with highly diverse characteristics, and employed different methodologies. Surgical techniques have also been extremely variable, and patient follow-up has been inconsistent (in terms of duration, endpoints and assessment modalities). Moreover, by its very nature, pelvic exenteration is an exceedingly complex surgical procedure requiring the oncologic surgeon to undergo a substantial learning curve in order to perform it correctly and with minimal morbidity. Surgical experience plays a crucial role in determining outcomes and can significantly influence study results.

The aim of this thesis is to clarify the outcomes that can be achieved through pelvic exenterations in patients with advanced pelvic malignancies. Furthermore, although certain prognostic factors have already been described in the literature [1], there is currently no patient-selection guideline capable of minimizing complications and optimizing oncologic outcomes—an aspect that will be addressed, at least in part, by the present work.

The primary hypothesis of the doctoral research is that certain characteristics related to the extent and histological type of the malignancy, as well as specific surgical-

technical factors, may be identified as being associated with favorable oncologic results (overall survival – OS, progression-free survival – PFS, patient quality of life – QoL).

The secondary hypothesis is that a series of prognostic factors for the occurrence of complications after pelvectomies—related either to the patient (comorbidities or preexisting/concomitant therapies, biological, paraclinical or genetic alterations) or to the tumor (location, histopathology, immunohistochemistry, etc.)—can be identified and used for case selection, an essential step for the success of this highly morbid procedure, which may significantly diminish patient quality of life postoperatively.

Research methodology – To achieve the aims of the doctoral thesis, the first step was an extensive review of the available national and international literature, which included not only existing data describing the procedure itself, its oncologic outcomes, and its impact on patients' quality of life, but also the evolutionary, pathogenetic, diagnostic and therapeutic aspects of all malignant tumors—and not only these—that may represent indications for pelvic exenteration. This process helped outline the current state of knowledge on the topic and allowed us to assess the expected impact that the doctoral research may have on advancing the field. The research plan was thus finalized. All bibliographic references were processed using a specialized software tool, Mendeley Reference Manager version 2.94.0, together with the associated browser (Mendeley Web Importer) and Microsoft Word (Mendeley Cite) add-ins—these tools being freely available online [2].

Following this literature review, the research plan was finalized, the study design and research instruments were established, and the patient cohorts and inclusion/exclusion criteria were defined. Patient data were collected from the electronic medical records and by reviewing physical medical charts from the hospital archives. Some data were obtained through direct or telephone interviews with patients or caregivers, who were informed about the purpose of the interview and/or signed informed consent to participate in the doctoral research. After building the database, all information was anonymized by removing any elements that could lead to patient identification.

The general objectives of the doctoral research were:

- descriptive-statistical characterization of patients undergoing pelvic exenterations and of the indications for these surgical procedures;
- identification of the types of complications associated with pelvic exenterations occurring in oncologic practice, along with their descriptive-statistical characterization and that of the patients affected;

- identification of risk factors influencing the occurrence of complications associated with pelvectomies;
- identification of factors influencing the curative potential of pelvectomies;
- evaluation of the impact of pelvectomies, as well as of postoperative complications, on oncologic outcomes and patient quality of life;
- development of a clinical guideline for patient selection to achieve an optimal risk–benefit ratio through pelvectomies.

The research progression followed a logical sequence, starting with an initial analysis of a small cohort of patients (intended to outline the basic concepts of the topic), continuing with an understanding of the socio-medical factors that underlie the high incidence of pelvic exenterations in Romania, validating the results in a larger patient cohort, complementing the analysis with aspects related to the psychosocial consequences of the intervention, and concluding with the development of a modern predictive clinical tool for optimal patient selection, with real practical applicability.

Study 1 represented the first stage, using data already available from a cohort of 132 patients operated between 2011 and 2017. The aim was to establish the basic premises: patient characteristics, surgical indications, complication types and the main determinants of survival. The analysis confirmed that pelvic exenteration, despite its high morbidity, can provide real survival benefits when radical R0 resection is achieved.

Building on these results, **Study 2** was motivated by the finding that gynecologic tumors—especially cervical cancer—had the most unfavorable prognosis after pelvectomy and often affect young patients, with major social implications. Romania is in a particular situation relative to the rest of Europe, with much higher incidence and mortality for this disease. The analysis included both epidemiological and clinical data from the Bucharest Oncology Institute and the perceptions and level of awareness among the female population, showing that late diagnosis is a consequence of systemic structural deficiencies (limited access to prevention and health education). Cervical cancer was selected as a paradigm, but similar motivations apply to digestive and urologic cancers.

Next, **Study 3** utilized the complete dataset (2008–2024, 229 patients) to conduct a comprehensive analysis of the entire population treated through pelvic exenteration at IOB. This stage allowed validation of the initial conclusions in a larger and more diverse cohort and evaluated quantitatively—and through descriptive statistics and correlation models—medical and oncologic outcomes (morbidity, mortality, OS, PFS) along with associated

prognostic factors. However, this analysis did not capture the human and psychosocial dimension of the intervention.

This limitation was addressed in **Study 4**, which investigated patient quality of life after pelvectomies. Through qualitative interviews and a narrative review of the recent international literature, the subjective patient experience was highlighted: difficulties related to body image, sexuality and social integration, as well as the sense of a "second chance" and relief of severe symptoms. The study demonstrated that the immediate postoperative negative impact may diminish over time, especially when psychological and family support are provided.

Finally, **Study 5** represented an innovative, forward-looking stage: the development of a clinical selection guideline based on a predictive model built using artificial intelligence algorithms. The analysis identified the preoperative factors that most accurately predict the likelihood of achieving an R0 resection—the most important determinant of survival. This tool may guide therapeutic decision-making, steering oncologic surgery toward personalized medicine and reducing the unnecessary risks of mutilating procedures without real benefit.

Personal contributions:

- analysis of the largest cohort published nationally, using all patients who underwent pelvic exenteration at the Bucharest Oncology Institute between 2008 and 2024 (Chapter 7);
- identification of key prognostic factors for survival, confirming the importance of radical R0 resection and revealing prognostic differences between primary and recurrent tumors, and between colorectal and gynecologic/urologic locations (Chapter 7);
- documentation of the particular situation of cervical cancer in Romania through a dual analysis—epidemiological and socio-medical—with relevance for public health policies (Chapter 6);
- integration of a qualitative perspective on quality of life, complementing medical data with an understanding of the human, psychological and social consequences of pelvectomies (Chapter 8);
- development of a predictive model based on artificial intelligence for patient selection—an original and innovative contribution with immediate clinical applicability and potential for integration into national and international guidelines (Chapter 9).

This thesis demonstrates that pelvic exenteration, although mutilating and associated with high morbidity, remains an indispensable procedure for patients with advanced or recurrent pelvic malignancies. Its success depends on correct patient selection, a multidisciplinary approach and appropriate postoperative support. The thesis also highlights the particularities of the Romanian healthcare system, where late diagnosis sustains the ongoing need for such radical surgical interventions.

The personal contributions encompass the successive analytical stages—clinical, epidemiological, socio-medical, qualitative and predictive—thus constructing an integrated view of pelvectomy, from its biological and surgical foundations to personalized medicine and patient-centered outcomes. These contributions are measurable and explicitly reflected in the chapters and paragraphs referenced, representing the author's original contribution to scientific knowledge in the field.

The work fully achieved its initial objectives, successfully addressing the research hypotheses: it demonstrated that there are oncologic, clinical and sociodemographic factors that decisively influence the success of pelvectomies, and provided a practical tool for guiding a more personalized therapeutic approach. Moreover, it offered a comprehensive analysis of the socio-medical motivations underlying the persistently high need for such highly invasive surgical procedures in Romania.

By integrating new available technologies, this work contributes to the modernization of Romanian oncology and marks a transition toward personalized, data-driven, safer and more effective cancer care.

Studies Conducted and Their Main Findings

Study 1 – Pelvectomies at IOB (Preliminary Experience)

For this study, all patients who underwent pelvic exenteration between January 2011 and December 2017 were considered eligible for inclusion (132 patients), regardless of indication (radical or palliative, malignant or benign disease, primary advanced pelvic cancer, recurrent disease, or synchronous pelvic malignancies). Some patients were included despite systemic disease dissemination, where pelvic exenteration had been indicated as a palliative procedure aimed at alleviating symptoms.

Data were collected through review of medical records, imaging, paraclinical tests, and histopathological reports. Operative details were obtained from surgical registries. Collected variables included: sociodemographic characteristics, comorbidities, indication

for pelvic exenteration, histopathological features, local and systemic disease dissemination, curative/palliative intent, operative duration, blood loss, length of hospital stay, peri- and postoperative complications, mortality, the need for and type of neoadjuvant/adjuvant therapy, and long-term outcomes such as survival intervals and time to recurrence/progression.

Assessment of patient characteristics, disease features, peri-/postoperative details, and complications was performed using data from all included cases. For oncological outcome analyses, only cases with histologically confirmed malignant disease were used.

Among the 132 patients included, the median age at the time of pelvic exenteration was 57.4 years (range 24–78), with most patients (51.52%) being older than 60. The female-to-male ratio was 1.93:1. One quarter of all patients resided in rural areas—an expected distribution, since limited access to healthcare services in rural settings is known to result in delayed diagnosis and more advanced disease at presentation. Considering the older age of many patients, comorbidities were potential risk factors. The most prevalent was arterial hypertension (present in nearly half of patients). Other comorbidities included diabetes mellitus (managed with oral antidiabetics or insulin), chronic kidney disease (typically resulting from ureteral obstruction by pelvic tumors and secondary hydronephrosis), and chronic pulmonary disease (associated with smoking habits and occupational/environmental exposures).

Pelvic exenteration was performed for malignant disease in most cases (127 patients): 65.15% had primary cancers, 28.03% had recurrent cancer, and 3.03% had synchronous multiple pelvic malignancies. Five patients underwent pelvic exenteration for benign conditions (complex fistulas between various pelvic organs).

The most common origin of malignant disease was gynecologic cancer, either locally advanced or recurrent (54.55%: 49 cervical, 12 endometrial, 9 ovarian, 2 vaginal). Pelvic exenteration was also indicated for colorectal cancer in 37 cases (28.03%), bladder malignancies in 21 cases (15.91%), and soft-tissue sarcomas in 2 cases (1.51%). The high proportion of gynecologic cancers reflects the case distribution in our institution (one-third of all major surgical procedures are performed for gynecologic malignancies). The most frequent histologic type was adenocarcinoma (approximately 45% of all cases), followed by squamous cell carcinoma. Nearly half of all tumors were poorly differentiated (G3), while only 10% were well differentiated—an expected finding, given the known association between poor differentiation and aggressive disease.

All patients were evaluated in a multidisciplinary tumor board, and neoadjuvant therapy was recommended and administered when appropriate. As a result, 56.06% of patients (74) received neoadjuvant treatment consisting of chemotherapy, radiotherapy, brachytherapy, or combinations thereof.

The indications for pelvic exenteration and the characteristics of malignant disease are summarized in Table 1.

Table 1. Indications for Pelvic Exenteration and Characteristics of Neoplastic Disease

Indication for exenteration	Primary disease	86 (65,15%)
	Recurrent cancer	37 (28,03%)
	Synchronous cancers	4 (3,03%)
	Benign disorders*	5 (3,79%)
Tumor origin	Cervical	49 (37,12%)
	Endometrial	12 (9,09%)
	Ovarian	9 (6,82%)
	Urinary bladder	21 (15,91%)
	Colo-rectal (including anal)	37 (28,03%)
	Others**	4 (3,03%)
Histologic type	Scuamo-celular carcinoma	48 (36,36%)
	Adenocarcinoma	59 (44,70%)
	Sarcom	4 (3,03%)
	Carcinom urotelial	21 (15,91%)
Degree of differentiation	G1	14 (10,61%)
	G2	56 (42,42%)
	G3	62 (46,97%)
Neoadjuvant therapy	Yes	74 (56.06%)
	No	58 (43.94%)

* Includes complex fistulas between pelvic organs; ** all other tumor types, including vaginal cancers and soft-tissue sarcomas.

Regarding the type of exenteration performed, in more than 50% of cases an anterior pelvectomy was required, while almost 30% of patients underwent a total pelvectomy (in 7 cases resection of the pelvic floor was necessary, whereas in 31 cases the resection was performed in a supralevator plane). The remaining patients underwent posterior exenteration. In 2 cases, lateral extension of the resection was necessary (segmental resection of the external iliac artery and/or vein, followed by vascular reconstruction).

A regional lymphadenectomy was performed in 92 patients (72.44%)—either bilateral pelvic, para-aortic, bilateral inguinal, or a combination thereof. Regional lymphadenectomy

was not required in 35 patients. Resection of additional extra-pelvic organs was necessary in 16.67% of cases and included segmental ileal resection (12 cases), appendectomy (2 cases), colectomy (2 cases), vulvectomy (1 case), omentectomy (4 cases), and splenectomy (1 case).

Every effort was made to achieve radical resection whenever possible. As a result, most procedures (76.38%) were carried out with curative intent, and only 30 patients underwent palliative procedures (in 17 cases the palliative intent was known preoperatively, while in 13 cases the histopathological result revealed an R1 resection, confirming the palliative nature of the intervention).

Digestive tract reconstruction was achieved in 63 cases, either through a colorectal anastomosis (the preferred option whenever feasible) or a terminal colostomy (when anastomosis was not possible due to inadequate vascularization of the anastomotic partners, poor tissue quality resulting from prior radiotherapy, or patient-related factors such as severe obesity or protein malnutrition). In 13 cases, the colorectal anastomosis was performed manually, and in 6 cases mechanically.

Urinary reconstruction was performed in 107 cases—bilateral cutaneous ureterostomy ("double-barrel" technique) in 39.25%, Bricker ileal conduit in 41.12%, and ileal neobladder in 19.63%.

No significant differences were observed in operative duration between radical and palliative procedures, nor between exenterations performed for primary versus recurrent cancers ($p < 0.342$ and $p < 0.566$, respectively). The mean operative time was 410 minutes (range 280–600 minutes). Blood loss was higher in cases with recurrent disease compared to primary cancer ($p = 0.05$). The median estimated intraoperative blood loss was 850 mL (range 350–1400 mL).

The median length of stay in the intensive care unit was 7 days (range 3–32 days), and the median total hospital stay was 17 days (range 10–54 days). Longer ICU admissions were associated with reinterventions ($p < 0.001$), septic complications ($p = 0.02$), and organ failure ($p < 0.001$).

Early morbidity and mortality were defined as events occurring within 30 days postoperatively, and severity was graded according to the Clavien–Dindo classification, where grades 1–2 represent minor complications, grades 3–4 represent major, potentially life-threatening complications, and grade 5 denotes death.

Minor complications occurred in 25 patients (18.94%), while major complications occurred in 29 patients (21.69%). Complications in the study cohort included medical events

(deep vein thrombosis, prolonged postoperative ileus, acute cardiac and pulmonary events, organ failure, pseudomembranous colitis, drug-related allergic reactions) and surgical events (postoperative hemorrhage, digestive and urinary fistulas, septic complications—peritonitis and intra-abdominal abscess, evisceration, and acute limb ischemia).

Early mortality occurred in 3 cases (2.72%) as a result of septic complications followed by multiorgan failure or acute cardiac events.

The intraoperative details and early morbidity and mortality outcomes following pelvic exenteration are summarized in Table 2.

Table 2. Intraoperative Findings and Early Morbidity and Mortality Outcomes Following Pelvic Exenteration

Type of exenteration	
Total pelvic exenteration without pelvic floor resection	31 (23,49%)
Infralevator total pelvic exenteration	7 (5,30%)
Anterior	69 (52,27%)
Posterior	25 (18,94%)
Curative intent	
Radical	97 (76,38%)
Paliative	30 (23,62%)
Limfodisecție	
Pelvic lymph nodes	85 (66,93%)
Para-aortic lymph nodes	21 (16,54%)
Inguinal lymph nodes	2 (1,57%)
Resection of extra-pelvic organs	
Yes	22 (16,67%)
No	110 (83,33%)
Reconstructive procedures of the digestive tract	63
Anastomoză colo-rectală	19 (30,16%)
Colostomie terminală	44 (69,84%)
Reconstructive urinary procedures	107
Cutaneous ureterostomy	42 (39,25%)
Bricker procedure	44 (41,12%)
Ileal neo-bladder	21 (19,63%)
Mean duration of the intervention (min)	410 min (range 280-600 min)
Mean blood loss (ml)	850 ml (range 350-1400 ml)
Mean duration of ICU stay (days)	7 zile (range 3-32 zile)
Mean duration of hospitalization (days)	17 zile (range 10-54 zile)
Morbiditatea și mortalitatea precoce	

Clavien-Dindo Gr. 1-2	25 (18,94%)
Clavien-Dindo Gr. 3-4	29 (21,69%)
Reinterventions	17 (12,88%)
Causes for early reinterventions	Obstruction, digestive/urinary fistulas, hemostasis, peritonitis/intra-abdominal abscess, acute lower limb ischemia
Mortality (Clavien-Dindo Gr. 5)	3 (2,72%)
Causes of early mortality	MSOF (Multiple Systems Organ Failure) secondary to sepsis, acute cardiac events

All resected surgical specimens were analyzed, and the histopathological reports were reviewed during data collection. Tumor size was larger in cases of recurrent cancer compared to primary tumors ($p = 0.05$). The radical nature of the exenteration was microscopically confirmed in 97 cases and disproven in 30 cases (among these, 13 procedures were initially intended to be curative, but the resection specimens demonstrated microscopic malignant residuals at the surgical margins). Radicality was more likely to be achieved when lateral tumor extension was absent—specifically, in the absence of vascular or bony invasion, or extensive parametrial or pararectal involvement ($p = 0.05$).

The results of the histopathological analysis of the resection specimens are summarized in Table 3.

Table 3. Histopathological Findings of Resected Specimens in Neoplastic Cases

Size of tumor	< 5 cm	38 (29,92%)
	≥ 5 cm	89 (70,08%)
Radicality	R0	97 (76,38%)
	R1	27 (21,26%)
	R2	3 (2,36%)
Lateral extension of tumor	Yes	23 (18,11%)
	Nu	104 (81,89%)
Ganglioni regionali invadați	Yes	95 (74,80%)
	Nu	32 (25,20%)
Perineural invasion	Yes	69 (54,33%)
	Nu	36 (28,35%)
	Unspecified	22 (17,32%)
Lymphovascular invasion	Yes	78 (61,42%)
	Nu	42 (33,07%)
	Unspecified	7 (5,51%)

After the intervention, all cases were re-evaluated within the multidisciplinary tumor board, and adjuvant therapy (chemotherapy, radiotherapy, immunotherapy, or combinations

thereof) was recommended for 93 patients. No significant difference was observed in the need for adjuvant treatment between primary and recurrent tumors ($p = 0.213$). The median postoperative follow-up period was 32 months (range 6–120 months). Follow-up ended either at the time of the patient's death or when the patient was no longer available for evaluation.

Local recurrences were observed in 37 patients after a median interval of 15 months. As expected, 30 of these were patients with known residual tumor tissue after exenteration (R1/R2 resection). Local recurrence rates were higher in patients with positive surgical margins ($p < 0.0001$) and in those operated on for recurrent malignant disease ($p = 0.03$). Systemic recurrence was documented in 21 patients after a median of 23 months. Among these, 13 patients already had systemic disease at the time of palliative pelvic exenteration performed for symptom control.

Long-term oncological outcome analysis showed a mean overall survival (OS) of 43.7 months and a mean recurrence-free survival (RFS) of 24.3 months. Within our cohort, two patients can be considered cured, as they remained alive 120 months after surgery. The most important determinants of OS in univariate analysis were R0 resection (52.6 months vs. 14.8 months in R1/R2 cases, $p < 0.001$), the primary tumor origin (48.6 months for colorectal cancer vs. 38.3 months for gynecologic cancer vs. 35.2 months for bladder cancer), and the primary nature of disease (49.1 months vs. 32.8 months for recurrent cancer, $p = 0.04$). Tumor size, histological type and grade, and perineural invasion did not significantly affect OS. The presence of lymphovascular invasion in resection specimens was associated with reduced OS ($p = 0.02$).

In our study, tumor size, histopathological type and grade, and perineural invasion did not significantly influence OS. The presence of lymphovascular invasion on resected specimens was associated with reduced OS, in line with previous research. As expected, long-term follow-up demonstrated that local recurrences were more likely in patients with residual tumor after exenteration (R1/R2 resection). Local recurrence rates were higher in patients with positive resection margins and in those treated for recurrent malignant disease. Systemic recurrence occurred after a median of 23 months, although our results may be influenced by the inclusion of patients with known metastatic disease undergoing pelvic exenteration for symptom relief.

A shorter disease-free survival is generally associated with recurrent disease; however, as an exception, colorectal tumors tend to show better survival outcomes compared to other recurrent or primary tumors [3,4]. Even in palliative settings, resection of the primary tumor

is associated with longer survival than minimally invasive alternatives (e.g., metal stent placement for locally advanced stenotic colorectal tumors) [5]. This can be explained by the fact that primary tumor removal eliminates the clinical uncertainty posed by the tumor (bleeding, infection, fistulization, and potential for systemic spread).

The strength of the study lies in its large cohort, which improves the statistical power. Moreover, all patients were selected from a single tertiary center and operated on by a limited number of highly trained oncologic surgeons, thereby minimizing the potential influence of the "learning curve" on R0 resection rates. Limitations include its retrospective nature and the high heterogeneity of the included patients, predisposing to type II statistical errors.

Pelvic exenteration, although a rational procedure for locally advanced, recurrent, or synchronous pelvic malignancies when other therapeutic options are absent or ineffective, remains associated with high morbidity. Nevertheless, a significant survival benefit is observed when an R0 resection is achievable. Additional prognostic factors for survival include the primary tumor origin (colorectal tumors being associated with higher survival rates and longer survival compared with non-colorectal tumors), the primary versus recurrent nature of disease (recurrent disease being associated with poorer outcomes), lateral tumor extension, and certain pathological features such as lymphovascular invasion.

Given the observed OS benefits and the ability to carefully select patients, we consider pelvic exenteration to be a safe and feasible procedure for locally advanced, recurrent, and synchronous pelvic malignancies, and it should be considered on an individualized basis.

Study 2 – Analysis of Socio-Demographic Factors Influencing the Need for Pelvic Exenteration

In a global context in which the trend is toward earlier diagnosis of neoplastic diseases—through the development of screening and prevention programs—it becomes essential to understand why, in Romania, these diseases continue to be detected at advanced stages, often forcing medical teams to opt for extreme procedures such as those addressed in this thesis. The medical care required for advanced malignancies consistently burdens the healthcare system and could be substantially reduced through coherent health policies. For these reasons, we considered it appropriate to analyze both the impact of late cancer diagnosis on the medical system and the specific causes underlying delayed detection in Romania, using cervical cancer as a model—given that it was the most frequent indication for pelvic exenteration in our cohort (37.12%). Cervical cancer was also selected because, in our study population, women under 40 years old with locally advanced cervical cancer

represented an overwhelming proportion (90.9%). Of course, similar causes of late diagnosis can be identified for other malignancies that commonly indicate pelvic exenteration, as they share the same socio-cultural and economic context.

The study consisted of two components.

The first component relied on descriptive statistical information extracted from the electronic database of the Bucharest Oncology Institute "Prof. Dr. Alexandru Trestioreanu," the largest oncology center in Romania and the main institution providing oncological care for approximately one-third of the national territory, serving a population of nearly eight million. We sought to assess the burden posed by cervical cancer among the pathologies treated in our hospital, placing these findings in the context of known global and European incidence and mortality rates, thereby evaluating the importance of this public health issue in Romania. For this purpose, we analyzed the institutional electronic database using ICD-10 code C53—Malignant neoplasm of the cervix uteri—as the filter and extracted data on the number of patients treated annually for cervical cancer between 2012 and 2022, the number of distinct hospitalizations required, the number of surgical procedures performed for this pathology, and the total number of hospitalization days.

Between 2012 and 2022, cervical cancer accounted for 17.97% to 29.56% of all cases treated in the Bucharest Oncology Institute. Between 15% and 30% of all surgical procedures performed in any given year were carried out for malignant cervical tumors. Most cases (>87% each year) were diagnosed at advanced stages (>stage Ib), requiring more than local treatment. Between 3.5% and 5.9% of the cervical cancer cases operated annually required extreme surgical procedures (such as pelvic exenteration) to ensure optimal treatment. This reality, combined with the significant comorbidity burden in many of these women (elderly age, cardiovascular, pulmonary, renal, or other chronic diseases), led to an increase in both the mean hospitalization duration per episode and the cost of managing each case. The mean length of stay was 7.62 days in 2022, 10.12 days in 2021, and 10.25 days in 2020, with extremes ranging from 1 to 56 days.

The cost per cervical cancer case has risen steadily in recent years, further straining an already underfunded health system. This cost has doubled over the last three years, reaching 12,149 RON per treated case in 2022 (compared with 5,146 RON per case in 2020). This amount represents the total sum paid by the hospital for medication, equipment, devices required for treatment, and hospitalization-related expenses (electricity, water, cleaning services, meals, etc.). The cost does not include salaries of the medical staff involved in managing the case. Each treated case is reported, and the state (the main healthcare insurer

for all Romanian citizens) reimburses the hospital a fixed amount calculated based on the case complexity index, regardless of any additional expenses generated by more complicated cases. Currently, the state reimburses less than 7,000 RON per cervical cancer case—an amount that has not increased in recent years. Consequently, under the current reimbursement model, each cervical cancer case creates a significant financial deficit for the hospital, jeopardizing the institution's ability to provide adequate care for future patients.

The second component of our study was a cross-sectional analysis of women participating in the National Cervical Cancer Screening Program during Papanicolaou testing campaigns performed with a mobile screening unit organized by the Bucharest Oncology Institute in the counties of Tulcea, Buzău, and Ilfov. A total of 528 women responded to a 14-item questionnaire assessing demographic characteristics, knowledge about screening and HPV vaccination, and access to cervical cancer–specific medical services.

The results showed that the exceptionally high incidence of advanced cervical cancer and the late presentation to medical care—often necessitating pelvic exenteration as the only therapeutic option—are due to a combination of factors related to both the dysfunctional healthcare system (non-functional screening and vaccination programs, lack of funding, limited accessibility to medical services for large segments of the population) and socio-cultural characteristics of the country (insufficient health education, cultural beliefs, and traditional attitudes).

This study focused on identifying the reasons for late diagnosis specifically in cervical cancer, but similar causes apply to other malignancies that may indicate pelvic exenteration. In Romania, colorectal cancer screening is also performed sporadically, with no population-based program in place. As with cervical cancer, colorectal cancer patients frequently present at advanced stages due to personal factors reflecting poor medical knowledge and limited access to preventive and screening services (absence of symptoms, financial barriers, distance from medical facilities, lack of information regarding available testing sites and modalities, fear of doctors/procedures, or fear of potential results).

The need for coherent and sustained awareness campaigns targeting both patients and healthcare professionals becomes evident. Changes in health policies and in the current reimbursement system could improve access to preventive and diagnostic services, ultimately reducing the burden of advanced malignancies and the need for radical procedures such as pelvic exenteration.

Study 3 – Pelvic Exenterations: Which Patients Are They Intended For, and What Outcomes Do They Achieve?

After accumulating substantial experience in pelvic exenterations at the Bucharest Oncology Institute since 2008, we decided to conduct a systematic evaluation of the outcomes obtained in an extended cohort, reflecting real-world clinical practice. This study included 229 consecutive patients who underwent pelvic exenteration between 2008 and 2024, representing the largest series reported in Romania to date.

The aim was to characterize, from a clinical and oncological perspective, the population undergoing this extreme procedure; to identify the tumor types most frequently involved; to evaluate surgical and oncological outcomes; and to correlate these parameters with survival. The included patients presented advanced pelvic tumors, most commonly of gynecologic origin (especially cervical cancer), colorectal cancer, and, to a lesser extent, urologic tumors. Approximately two-thirds of the cases were locally advanced primary tumors, with the remainder representing pelvic recurrences. Notably, there was a high proportion of young patients with advanced cervical cancer, reflecting the epidemiological particularities of Romania.

Surgical outcomes and complications:

The procedures were complex, often requiring multivisceral resections and, in some cases, extensive pelvic reconstruction. An R0 resection was achieved in over 60% of cases, and this variable showed a strong correlation with overall survival. Postoperative complications occurred in approximately 40% of cases, with a lower proportion of severe complications (Clavien-Dindo ≥ III). Perioperative mortality remained low, under 5%, highlighting both the maturation of the surgical team and the adequacy of preoperative patient selection.

Oncological outcomes:

Median overall survival was 31.5 months, with a 3-year survival rate of approximately 46% for the entire cohort. Patients with primary tumors had significantly better survival compared with those with pelvic recurrences (39 months vs. 19 months). Colorectal tumors were associated with the most favorable prognosis (median survival of 49 months), whereas gynecologic tumors had the poorest outcomes (25 months). Achieving negative surgical margins (R0) increased survival to more than 40 months, compared with only 14 months in cases with positive or microscopically invaded margins (R1/R2).

Study conclusions:

This study demonstrates that pelvic exenteration, although associated with significant morbidity, remains an intervention with substantial oncological value in carefully selected patients. The best outcomes were seen in primary tumors, especially of colorectal origin, and when an R0 resection was feasible—emphasizing the importance of appropriate patient selection and multidisciplinary collaboration.

Furthermore, this analysis enabled the identification of clinical parameters with predictive value, subsequently integrated into the development of a predictive model for complications and survival (detailed in Study 5). These data underscore the need for specialized high-volume centers for such major procedures, where accumulated surgical expertise contributes decisively to reducing risks and optimizing therapeutic outcomes.

Study 4 – Quality of Life of Patients After Pelvic Exenteration

After the extensive quantitative analysis of the cohorts of patients who underwent pelvic exenteration (Study 3), the author aimed in this chapter to explore a dimension often overlooked in hard oncological research: the subjective experience of the patient after a radical intervention. Study 4 therefore aimed to provide a contextual and in-depth understanding of the impact on quality of life (QoL), using a dual approach: semi-structured interviews with 5 patients selected from the operated cohort, at distance from the intervention and able to reflect on their experience, and a narrative review of the recent international literature regarding QoL after pelvic exenteration.

The 5 patients included were strategically selected to reflect the diversity of cases: different ages, diverse tumor pathologies, different types of reconstruction. The interviews were analyzed thematically and highlighted a series of recurrent dimensions of suffering and postoperative adaptation:

• Loss of bodily identity and of basic physiological functionality (urination, defecation, sexuality);

• Social isolation and difficulties in professional reintegration;

• Reconstruction of the personal meaning of illness and healing;

• The fundamental role of the family in the process of emotional adjustment;

• Lack of structured psychological support, identified as a major gap in the postoperative pathway.

Patients described pelvic exenteration as a “life-saving” intervention, but with a profound personal cost. Although some managed to adapt, all expressed the need for psychological support, counselling, and normalization of everyday life.

To place the qualitative results in a broader scientific context, the author conducted a narrative analysis of the international literature from the last 10 years, identifying 18 relevant articles that addressed QoL after pelvic exenteration. Most studies used validated instruments such as the EORTC QLQ-C30, but varied in the depth of evaluation.

A methodological heterogeneity emerged, as well as a lack of longitudinal data, which makes a universal conclusion difficult. However, common trends confirm that patients show low scores for physical, social, and sexual functioning, especially during the first postoperative year. The psychological dimension is rarely assessed in depth, and post-exenteration rehabilitation models are fragmented and rarely implemented in a standardized manner.

Conclusions of the study:

Pelvic exenteration produces a significant impact on quality of life, far beyond what can be quantified numerically. The personal experience of the patient—centered on loss, adaptation, and meaning—must be integrated into the therapeutic decision. The lack of psychological and social support programs in Romania represents a major gap in postoperative care. The literature review supports the qualitative observations and highlights the need for standardizing QoL assessment and for an integrative approach to the care of patients undergoing pelvic exenteration.

Study 5 – Developing a Clinical Guide for Selecting Patients in Order to Achieve an Optimal Risk–Benefit Ratio for Pelvic Exenteration

After the in-depth exploration of the impact of pelvic exenteration on survival (Study 3) and quality of life (Study 4), I formulated a key question: How can we better select the patients who will benefit from pelvic exenteration, reducing risks and increasing the chances of oncologic success and functional recovery? Study 5 had a dual purpose: 1. To describe the process of developing a predictive model for achieving complete resection based on preoperative factors, using machine-learning algorithms, considering that negative resection margins are the most important determinant of overall survival and progression-free survival; and 2. To derive from this model a set of clinical selection factors that can form the basis of a clinical guide for selecting patients who will achieve an optimal risk/benefit ratio after pelvic exenteration.

A completed and cleaned database was used, including 229 consecutive pelvic exenteration cases performed between 2008–2024. The target variable (to be predicted),

named Marg_rez, is a binary variable encoding with 0 a negative resection margin and with 1 a carcinomatosis-infiltrated resection margin.

As predictive factors, exclusively variables available prior to surgery were selected, divided into 6 categories:

- Demographic: age, sex, environment of origin;
- Oncologic: tumor type (primary/recurrent), tumor etiology (gynecologic, urologic, digestive), TNM characteristics, disease stage, presence of pelvic peritoneal metastases (resectable) and metastases in other sites;
- Histologic: tumor differentiation grade (G), presence of lymphovascular and perineural invasion on biopsy samples (LVI and PNI), presence of peritumoral lymphocytic infiltrate;
- Preoperative imaging: presence of regional tumoral lymphadenopathies, invasion of the pelvic floor, lateral extension of disease and vascular–nervous involvement, extra-pelvic extension of disease, presence of ascites;
- Therapeutic: neoadjuvant radiotherapy and chemotherapy, response to neoadjuvant therapy, and the emergency/elective character of the intervention;
- Biologic: preoperative serum markers – Hg, leukocytes, neutrophils, platelets, glucose, urea, creatinine, AST, ALT, electrolytes, albumin, APTT, PT, AP, INR.

In the attempt to predict the achievement of an R0 resection, I used two types of machine-learning algorithms:

- Random Forest (RF) – an algorithm based on decision trees trained on bootstrapped subsets of data (an initial number of 500 trees was used, with later adjustments through cross-validation). This model is tolerant to noise and can handle heterogeneous continuous or categorical variables.
- XGBoost (Extreme Gradient Boosting) – a gradient boosting algorithm that builds sequential trees, each new tree correcting the errors of previous ones, known for high performance in classification, especially on datasets with many predictors and multiple non-linear relationships. Key parameters (learning rate, max depth, subsample, colsample_bytree) were optimized through a limited grid search, considering the relatively small size of the dataset.

Applying the two machine-learning models (Random Forest – RF and XGBoost – XGB) to the analyzed cohort revealed notable differences in their ability to predict radical resection (R0).

The RF model achieved the highest overall accuracy (83.6% vs. 80% for XGB).

However, class-level analysis showed that RF failed to correctly identify cases with positive margins (R1/R2 resection), having a recall of 0 for this category. Practically, RF predominantly predicted R0 resections, which explains the apparently higher accuracy, but it is completely "blind" when it comes to identifying the category of interest – cases in which radical resection is not possible. This fact massively reduces its clinical relevance.

In contrast, XGB demonstrated a more balanced discriminatory capacity, achieving a recall of 33% for R1/R2 cases and a superior ROC-AUC (0.792 vs. 0.767 for RF). Although sensitivity remains moderate, this model better identified patients at high risk for incomplete resection, an aspect of major practical importance.

Table 4. Comparative summary of the performance indicators of the predictive models

Indicator	Random Forest	XGBoost
Global accuracy	0.836	0.800
AUC-ROC	0.767	0.792
Precision (R0)	0.836	0.872
Sensitivity (R0) - recall	1.000	0.891
Specificity (R0)	0.000	0.333
F1-score (R0)	0.911	0.882
Precision (R1/R2)	0.000	0.375
Sensitivity (R1/R2) - recall	0.000	0.333
Specificity (R1/R2)	1.000	0.891
F1-score (R1/R2)	0.000	0.353
Weighted accuracy	0.500	0.612

The analysis of the importance of preoperative variables for the predictive power of the models revealed different profiles between RF and XGB. RF prioritized preoperative biological parameters (serum values of APTT, PT, INR, fibrinogen, albumin, transaminases, urea and creatinine, electrolytes, blood glucose, hemoglobin, platelets and leukocytes), suggesting an influence of the patient's biological status on surgical radicality – a fact which rarely has a real counterpart in oncologic surgical practice and which explains the model's specificity of 0 (the inability to correctly identify cases with carcinomatosis-infiltrated resection margins). The parameters considered important by RF are rather relevant for the general surgical risk and for the risk of developing postoperative complications than for surgical radicality.

In contrast, although XGB also takes into account certain biological parameters (such as preoperative platelet count or urea level), this model focuses on predictive factors related to the type and extent of the treated tumor, the presence of complications at the time of surgery, and the patient's comorbidities/pathological history (e.g., diabetes mellitus, heart failure, chronic kidney disease or other neoplasms).

Thus, aggressive tumors (with poor differentiation grade), with preoperatively known systemic dissemination (metastatic disease), showing extra-pelvic extension or intraperitoneal fluid on preoperative imaging, recurrent tumors, or tumors of gynecologic origin were associated with a low rate of achieving R0 resection margins. Similarly, a history of pelvic radiotherapy or abdominal surgery, as well as the presence of complex fistulas between pelvic organs, were associated with low rates of complete resection, probably due to the fibrotic–inflammatory changes that develop and make dissection of tissue planes more difficult. The extent of the surgical resection also influences the achievement of negative margins – both total pelvectomy and the need to resect extra-pelvic organs were associated with lower R0 resection rates.

Surprisingly, lateral extension with infiltration/invasion of the iliac vascular axis and extension to the pelvic floor were not negative predictive factors for obtaining clear margins. This is probably explained by the possibility of resecting these structures by experienced oncologic surgeons. Achieving radicality appears to depend more on the absence of neoplastic extension to unresectable structures. The algorithm clearly differentiated between irreducible factors (tumoral lymphadenopathy, systemic dissemination, diffuse extensions) and technically resectable factors (vessels, pelvic floor), assigning predictive value for R0 resection only to the former. From the perspective of patient selection, the result of the XGB model suggests that the preoperative presence of vascular or pelvic floor infiltration/invasion should not automatically exclude a patient from pelvic exenteration, provided that the surgical team has the necessary experience in performing such resections.

It is important to underline the main point of convergence of the two models, namely the identification of lymphatic extension of the neoplastic disease on preoperative imaging as the main determinant of the possibility of achieving an R0 resection. Locoregional lymphatic invasion is a classic indicator of tumor spread and aggressive tumor biology. The absence of imaging-visible lymphadenopathy suggests locally limited disease, which significantly increases the chance that the tumor can be completely resected. The fact that both RF (more "sensitive" to biological data) and XGB (more "attentive" to anatomical and oncologic factors) place this predictor first in the importance ranking shows that its signal is

extremely strong and robust, regardless of the algorithmic approach. This convergence increases confidence in the validity of the predictor and suggests that it should be the central element in a clinical patient selection guide. The absence of lymphadenopathy can be used as a major eligibility criterion for pelvic exenteration with curative intent, while imaging-visible lymphadenopathy may tip the therapeutic decision towards postponing surgery or replacing it with neo-adjuvant multimodal strategies (radio-chemotherapy) and subsequent re-evaluation. Considering that R0 margins are the most important determinant of survival, the preoperative absence of lymphadenopathy can be regarded as an indirect imaging biomarker of favorable prognosis. Large pelvic exenteration studies (for example, Höckel 2012, Colombo 2019) have shown that patients without extensive nodal invasion at diagnosis have higher rates of radical resection and long-term survival. The trained models reproduce this finding from our own database, which provides internal validation and confirms that the predictions are aligned with clinical and biological reality.

The results of our study suggest that tree-based models have different performance profiles depending on the type of clinical signal they capture. Random Forest is robust and predominantly "sees" biological and metabolic status, but tends to ignore the oncologic dimension of prediction. This tendency explains its apparently better overall performance but the complete lack of sensitivity for R1/R2 cases. From a clinical perspective, such a model is insufficient, since the surgical decision fundamentally relies on the ability to anticipate incomplete resections. Through its regularization mechanisms and its capacity to capture complex interactions, XGBoost managed to more faithfully incorporate clinico-anatomical signals. Thus, it better reflects practical reality, where loco-regional tumor extension and invasion of critical structures are the major determinants of surgical radicality. Comparatively, XGB aligns more closely with the available literature and with oncologic practice – anatomical factors and tumor extent determine surgical radicality, and recognizing them is essential for the correct selection of patients who will benefit from an optimal risk/benefit ratio after pelvic exenteration. XGB is suitable for oncologic prediction (the likelihood of R0 resection) and, therefore, for integration into a clinical patient selection guide. Although its performance in identifying cases with positive margins is not optimal, it provides a far more useful basis for decision-making than RF, which completely misses this aspect. In addition, the profile of important factors identified by XGB can form the foundation for developing a clinical selection guide, integrating imaging, anatomical and comorbidity elements into a preoperatively applicable risk matrix.

Based on the predictive elements identified by XGB, in Table 5. I propose the following algorithm for patient selection and therapeutic decision-making:

Table 5 – Patient selection guide according to the probability of achieving an R0 resection

Category	Clinical profile	Recommended action
„R0-friendly" Cases	No radiologically detectable loco-regional lymphadenopathy No extrapelvic extension Well- or moderately-differentiated primary tumors	Standard operative plan; High likelihood of achieving a radical (R0) resection
„Conversion" Cases	Partially reversible adverse factors: recurrent or poorly differentiated tumors (G3), limited peritoneal dissemination, post-radiotherapy sequelae No diffuse invasion or bulky lymphadenopathy	Neoadjuvant therapy (radio-chemotherapy), imaging reassessment, extended multidisciplinary board discussion. R0 achievable after conversion
Cases with low probability of obtaining R0	Regional lymphadenopathy present Ascites, diffuse extrapelvic extension Systemic metastases or lack of response to neoadjuvant therapy	Full restaging. Palliative systemic treatments. Possible conversion-therapy trial. Avoid mutilating pelvic exenteration when realistic chances of R0 are absent.

Conclusions:

The absence of radiologically visible regional lymph nodes emerged as the most important predictor of achieving an R0 resection, confirming that careful assessment of loco-regional extension remains the cornerstone of patient selection for pelvic exenteration. The results of the models show that other factors—such as vascular–nervous extension or invasion of the pelvic floor—although they increase technical complexity and morbidity, are not absolute limiting factors, since these structures can be resected with preserved chances of obtaining negative margins when the patient is treated in a high-experience center.

From this perspective, classifying patients into "R0-friendly," "conversion," and "low likelihood of upfront R0" categories provide a practical decision-making framework. It integrates not only raw anatomical data but also biological, histological, and treatment-response characteristics, enabling a multidimensional approach to patient selection.

In conclusion, pelvic exenteration should be viewed as a procedure that retains its relevance only when the probability of obtaining an R0 resection is realistic. In cases with

low likelihood of radicality, shifting toward systemic or palliative treatments is preferable to avoid unnecessary morbidity. The proposed classification based on the XGBoost model represents a step toward developing a structured clinical guide that ensures an optimal risk–benefit ratio and supports therapeutic decisions within a multidisciplinary framework. Although AI-based predictive models developed to date in pelvic oncology still show moderate performance, they can assist the decision-making process by identifying subtle patterns that anticipate the probability of achieving R0. In the future, combining these models with advanced imaging algorithms and multicenter databases could enable the development of even more refined selection guides, contributing to personalized surgical decision-making and maximizing patient prognosis.

References

[1] Radwan RW, Jones HG, Rawat N, Davies M, Evans MD, Harris DA, et al. Determinants of survival following pelvic exenteration for primary rectal cancer. British Journal of Surgery 2015;102:1278–84. https://doi.org/10.1002/BJS.9841.

[2] Download Mendeley Reference Manager For Desktop Windows | Mendeley n.d. https://www.mendeley.com/download-reference-manager/windows (accessed March 9, 2024).

[3] Pawlik TM, Skibber JM, Rodriguez-Bigas MA. Pelvic Exenteration for Advanced Pelvic Malignancies. Ann Surg Oncol 2006;13:612–23. https://doi.org/10.1245/ASO.2006.03.082.

[4] Zoucas E, Frederiksen S, Lydrup ML, Månsson W, Gustafson P, Alberius P. Pelvic exenteration for advanced and recurrent malignancy. World J Surg 2010;34:2177–84. https://doi.org/10.1007/S00268-010-0637-7.

[5] Rotaru V, Chitoran E, Gullo G, Mosoiu DV, Simion L. Self-Expanding Metal Stents as an Alternative to Palliative Surgery in Advanced Obstructive Colorectal Cancer—A Systematic Review and Meta-Analysis. J Clin Med 2025;14:4339. https://doi.org/10.3390/jcm14124339.

Listă cu lucrări științifice publicate

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1. Rotaru, V., Chitoran, E., Zob, D.-L., Ionescu, S.-O., Aisa, G., Andra-Delia, P., Serban, D., Stefan, D.-C., & Simion, L. (2024). **Pelvic Exenteration in Advanced, Recurrent or Synchronous Cancers—Last Resort or Therapeutic Option?** Diagnostics, 14(16), 1707. DOI: 10.3390/diagnostics14161707; PMCID: PMC11353817; PMID: 39202196.
https://doi.org/10.3390/diagnostics14161707
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2. Rotaru V, Chitoran E, Gelal A, Gullo G, Stefan D-C, Simion L. **Living After Pelvic Exenteration: A Mixed-Methods Synthesis of Quality-of-Life Outcomes and Patient Perspectives.** Journal of Clinical Medicine. 2025; 14(18):6541.
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3. Simion, L.; **Rotaru, V.;** Cirimbei, C.; Gales, L.; Stefan, D.-C.; Ionescu, S.-O.; Luca, D.; Doran, H.; Chitoran, E., **Inequities in Screening and HPV Vaccination Programs and Their Impact on Cervical Cancer Statistics in Romania.** Diagnostics 2023, 13, 2776.
DOI: 10.3390/ diagnostics13172776; PMCID: PMC10486539; PMID: 37685314.
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1. Rotaru, V.; Cirimbei, C.; Simion, L.; Ştefan, D.C.; Tănase, B.; Luca, D.C.; Chitoran, E. **Pelvic exenteration – between history and future**. First published: 21 octombrie 2022. Editorial Group: MEDICHUB MEDIA. DOI: 10.26416/OnHe.60.3.2022.7151.
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First author – Type of article: Review (Chapters 1 and 2)