Research Square

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Circulating Tumor cells detection by liquid biopsy during early-stage cervical cancer surgery: a pilot study

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Abstract

Background

The recurrence of early-stage cervical carcinoma (CC) (about 10%) might be due to disseminated tumor cells. This pilot study aimed to assess perioperative dissemination of circulating tumor cells (CTCs) into peripheral blood during surgery for early-stage CC and evaluate the feasibility of their detection.

Methods

In this bicentric prospective study, 11 patients undergoing laparoscopic resection of histologically confirmed FIGO stage IA1 to IB2 CC were included. CTCs were enumerated using the CellSearch® system in peripheral blood samples collected (i) preoperatively (T0), (ii) after pneumoperitoneum creation (T1), and (iii) before colpotomy (T2). The primary outcome was perioperative CTC detection (T1 or T2) and secondary outcomes included recurrence-free survival.

Results

CTCs were detected only peroperatively in 3/11 patients (27.3%; 95% CI: 7.3–60.7). One patient (9.1%) had 2 CTCs detected at T1 and two patients (18.2%) had CTCs detected at T2 (50 and 2 CTCs respectively). Among patients with CTCs, two had an epidermoid carcinoma and one an adenocarcinoma; they had stage IA1, IA2, and IB1 respectively. Histopathological examination of hysterectomy specimens revealed residual tumor in 3/11 patients (27.3%), including one CTC-positive patient. After a median follow-up of three years, one recurrence (9.1%) occurred, in a patient without perioperative CTC detection.

Conclusions

This pilot study demonstrates the feasibility of CTC detection in peripheral blood during surgery for early-stage CC. The prognostic and therapeutic values of CTCs released during cervical cancer surgery warrant further investigation.

Trial Registration:

ClinicalTrials.gov, NCT04770090, registered on 25 february 2021.

Introduction

Despite substantial reductions in incidence following the implementation of screening and HPV vaccination programs, cervical cancer continues to represent a major cause of cancer-related morbidity and mortality worldwide. Indeed, according to GLOBOCAN 2022, cervical cancer ranked fourth among cancers in women, accounting for approximately 660,000 new cases and 348,000 deaths worldwide(1). Despite advances in prevention and treatment, cervical cancer remains associated with substantial mortality, largely driven by disease recurrence and metastatic progression(1). Recurrence in early stages occurs in around 10% of cases, mostly within 3 years, and thus remains a major clinical challenge(2).

Radical surgery remains the cornerstone of treatment for early-stage cervical cancer(3, 4). Minimally invasive surgery was widely adopted because of its perioperative benefits before its oncological safety was questioned(3, 4). The publication of the LACC trial and subsequent observational studies challenged this approach by reporting poorer disease-free outcomes following minimally invasive radical hysterectomy compared with open surgery(3, 4). Various mechanisms have been suggested to account for these findings, particularly tumor manipulation by uterine manipulators and differences in colpotomy techniques(3). In prostate cancer, tumor mobilization during biopsies has been shown to increase circulating tumor cell (CTC) counts in blood, which were significantly correlated with poorer progression-free survival (PFS)(5). In early-stage cervical cancer, radical hysterectomy by laparotomy or laparoscopy both tended to increase the expression of CTC markers (cytokeratin 19 and 20 and squamous cell carcinoma antigen)(6). In addition, the potential role of pneumoperitoneum on the dissemination of CTCs has also been suggested to explain the poorer prognosis associated with laparoscopy(6, 7). Whether CO_2 insufflation facilitates hematogenous tumor-cell dissemination remains uncertain, highlighting the need for further mechanistic investigations(7).

Circulating tumor cells have attracted considerable interest in oncology over the past two decades. Large prospective studies and meta-analyses have consistently demonstrated the prognostic and predictive value of CTC detection in the response to treatment of metastatic breast, prostate and colon cancers (5, 8–10). Across these studies, detectable CTCs consistently predicted shorter progression-free and overall survival(OS). CTCs detected by the CellSearch system have also been identified as independent prognostic markers of PFS and OS in patients with non-metastatic breast cancer(11), while in non-metastatic colorectal cancer, a CTC count as low as one CTC/7.5 mL of blood was significantly associated with shorter OS(12).

Only a limited number of studies have investigated the detection of CTCs and their prognostic and clinical significance in cervical cancer, although their presence appears to be associated with poorer PFS(13, 14).

The aim of this pilot study was to evaluate the dissemination of CTCs during early-stage cervical cancer surgery on peripheral blood samples.

Materials and Methods

Study design

This bicentric exploratory study was conducted at the departments of gynecological surgery of the Montpellier and Nimes University Hospitals from November 2021 to June 2023 (ClinicalTrials.gov Identifier: NCT04770090). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and applicable national regulations governing clinical research. The study protocol was reviewed and approved by Ethics Committee IDF11 (Ile-de-France XI SAINT-GERMAIN-EN-LAYE), Approval No. 2020-A02456-33), Date: 05/11/2020). Written informed consent was obtained from all participants prior to their inclusion in the study. All participants were informed about the objectives, procedures, potential risks, and benefits of the research, and their right to withdraw from the study at any time without consequences. The study was registered in a public clinical trials registry (Registration No. NCT04770090, date 25/02/2021).

Patient recruitment

Eligible patients were invited to participate in the study during the preoperative consultation at the study centers. Patients aged 18 years or older with histologically confirmed primary FIGO stage IA1 to IB2 epidermoid carcinoma or adenocarcinoma, eligible for immediate (or post-brachytherapy) surgical treatment, by laparoscopy, were eligible. All participants underwent a pelvic MRI.

Patients with advanced stage disease, laparotomy, or other concomitant cancers were not included, as well as pregnant or breastfeeding women or those refusing to participate.

Surgical procedure

Surgical procedures were performed according to institutional standard practice and followed a standardized protocol across all participating centers. During minimally invasive surgery, pneumoperitoneum was created using carbon dioxide insufflation, maintaining the intra-abdominal pressure at or below 15 mmHg. A systematic exploration of the abdominal cavity was undertaken to rule out extra-pelvic disease, and peritoneal washings for cytological analysis were obtained at the beginning of the procedure. When indicated, nodal assessment, including sentinel lymph node biopsy with or without subsequent pelvic lymphadenectomy, was completed before radical hysterectomy. To minimize the risk of intraoperative tumor dissemination, the vaginal cuff was closed by vaginal route prior to uterine resection. All operations were performed without the use of a uterine manipulator. Resected specimens were subsequently submitted for definitive histopathological examination..

Blood sampling

The perioperative blood sampling protocol was based on a previously established methodology developed by our group and reported by Francini et al(7). Peripheral venous blood was collected at three predefined perioperative time points to evaluate circulating tumor cells. An initial 20-mL sample was obtained immediately before surgery, prior to the patient's transfer to the operating room (T0). Subsequent samples were collected after establishment of the CO_2 pneumoperitoneum (T1) and following division of the uterine pedicles, immediately before colpotomy (T2) (Fig. 1). At each collection,

blood was distributed into two 10-mL CellSave Preservative Tubes (Menarini Silicon Biosystems, Bologna, Italy). All specimens were maintained at room temperature and transported without delay to the Laboratory of Rare Human Circulating Cells (LCCRH) at Montpellier University Hospital (France) for subsequent analysis

CTC Enumeration

CTC analysis was performed using the same standardized methodology previously established by our group and reported by Francini *et al*(7). Blood samples were processed within 96 hours of collection using the CellSearch® platform with the dedicated CTC Kit (#7900001, Menarini–Silicon Biosystems, Bologna, Italy), following the manufacturer's instructions. The CellSearch® system represents the only FDA-cleared assay currently available for CTC enumeration in patients with metastatic breast, prostate, and colorectal cancers(15). Briefly, CTCs were enriched through immunomagnetic separation based on epithelial cell adhesion molecule (EpCAM) expression using antibody-coated magnetic particles. Following enrichment, cells were fluorescently labeled with antibodies targeting cytokeratins 8, 18, and 19, while leukocytes were identified through CD45 staining and excluded from analysis. Nuclear staining was performed using 4',6-diamidino-2-phenylindole (DAPI). The enriched and immunostained cell fraction was subsequently maintained within a magnetic field and analyzed by automated scanning. Final CTC identification and enumeration were performed by trained investigators (AP, LC).

Objectives and outcomes

The primary objective was to assess the perioperative dissemination of CTCs into peripheral blood during surgical treatment of early-stage cervical cancer. The primary outcome was a CTC-positive blood sample during surgery (i.e. at T1 or T2). At T0, a blood sample of 20 mL was considered positive when at least 1 CK(+), DAPI(+), CD45(−) cell was detected (15). At T1 and T2, a blood sample of 20 mL was considered positive when at least 1 CK(+), DAPI(+), CD45(−) cell was detected (in case of negative T0 sample), or if there was an increase of at least one cell compared with T0 (in case of positive T0 sample).

The secondary objective was to evaluate the prognostic impact of intraoperative CTC detection, as assessed by recurrence-free survival.

Statistical analysis

A target sample size of 20 patients was planned for this pilot study in the absence of available data on CTC detection in cervical cancer. During the inclusion period, new guidelines on cervical cancer management were published, recommending the laparotomy approach (16). Consequently, patient recruitment was prematurely discontinued. Nevertheless, all included patients were followed up as initially planned in the protocol to assess recurrence-free survival.

All analyses were performed on the entire study population. Given the small sample size, only descriptive analyses were conducted, both overall and according to CTC detection status.

Patient characteristics were described using median and range (minimum-maximum) for quantitative variables and counts and percentages for categorical variables. The primary outcome was described using number and frequencies (n, %) along with 95% confidence interval (95% CI). The number of recurrences was reported descriptively; however, no survival analysis was performed due to the limited sample size. All statistical analyses were performed using R (version 4.3.1) by the Clinical Research and Epidemiology Unit of Montpellier University Hospital, France.

Results

Patient cohort

A total of eleven patients meeting the inclusion criteria were included. Their clinicopathological characteristics are summarized in Table 1. The median age was 45 years [range: 33–75]. FIGO stage was IA1 in one patient (9.1%), IA2 in two patients (18.2%), IB1 in six patients (54.6%) and IB2 in two patients (18.2%). One patient (9.1%) received preoperative brachytherapy. Cervical cancer was primarily diagnosed by conization in 9 patients (81.8%) and by biopsy in two patients (18.2%). Pelvic lymph nodes were dissected in nine patients (81.8%). The median surgery duration was 240 minutes (range: 92–322). The planned total blood volume for CTC detection and analysis was successfully collected during peripheral venous sampling, with no complications reported.

Table 1
Patients' characteristics

Characteristics	Population (n = 11)
Age, *median (min, max)*	45 [33 ; 75]
BMI (kg/m²), *median (min, max)*	24.5 [21.3 ; 35.4]
Menopausal Hormonal status, *n (%)*	3 (27.3)
Preoperative Brachytherapy, *n (%)*	1 (9.1)
Histology, *n (%)*	
Epidermoid Carcinoma	9 (81.8)
Adenocarcinoma	2 (18.2)
FIGO stage, *n (%)*	
A1	1 (9.1)
A2	2 (18.2)
IB1	6 (54.6)
IB2	2 (18.2)
Surgery duration (min), *median (min, max)*	240 [92 ; 322]
Residual tumor, *n (%)*	3 (27.3)
Abbreviations: BMI: body mass index, FIGO: Federeration Internationale de Gynecologie et Obstétrique.	

CTC enumeration before, during and after surgery

Results of CTC detection at each time point are shown in Fig. 2. CTCs were not detected in preoperative samples (T0). Conversely, peroperative samples (T1 or T2) were positive in 3/11 patients (27.3%, 95% CI: 7.3 ; 60.7). After pneumoperitoneum (T1), one patient (9.1%) had two CTCs detected (one in each tube). During open surgery (T2), CTCs were detected in two patients (18.2%): one with a cluster of at least 50 CTCs and one with two CTCs (one in each tube) (Fig. 3).

Table 2 summarizes the clinicopathological characteristics of patients with and without CTC detection. Among the three CTC-positive patients, two had epidermoid carcinoma and one adenocarcinoma, with stage IA1, IA2, and IB1 respectively. Histopathological examination of hysterectomy specimens revealed the presence of residual tumor in three patients (27.3%), including one with CTCs.

Table 2
Clinicopathological features of patients with and without CTC detection

	CTC Detection	
	Negative (n = 8)	**Positive (n = 3)**
Age (years), median (min ; max)	43 (33 ; 48)	53 (36 ; 75)
Surgery duration (min), median (min ; max)	244 (162 ; 298)	223 (92 ; 322)
Histology, n (%)		
Epidermoid Carcinoma	7 (87.5)	2 (66.7)
Adenocarcinoma	1 (12.5)	1 (33.3)
FIGO stage, n (%)		
A1	0 (0)	1 (33.3)
A2	1 (12.5)	1 (33.3)
IB1	5 (62.5)	1 (33.3)
IB2	2 (25.0)	0 (0)
Residual tumor		
n, (%)	2 (25.0)	1 (33.3)
size *(individual values)*	3 mm;17mm	5 mm
Abbreviations: FIGO, Federation of Gynecology and Obstetrics		

Recurrence-free survival

All eleven patients were followed up until three years. Recurrence occurred in one patient (9.1%) who had no CTC detected during surgery (T1/T2). This was the patient with the largest residual tumor at the time of surgery. The recurrence was locoregional, with no evidence of local relapse or distant metastasis. The patient was treated with surgery and chemotherapy.

Discussion

The objective of this pilot study was to explore the presence and perioperative dynamics of 0CTCs in peripheral blood during surgery for early-stage cervical cancer. We showed that CTCs can be identified in intraoperative blood samples, suggesting that surgical procedures may provide an opportunity for real-time assessment of tumor cell dissemination. Further studies are needed to determine the prognostic implications of CTC detection and its potential association with recurrence outcomes.

Previous studies have reported highly variable rates of CTC detection in the peripheral blood of patients with cervical cancer, ranging from 26% to 90% (13, 14, 17–20). Such heterogeneity may be explained by differences in patient populations, tumor characteristics, disease stage, and the analytical methods used for CTC identification. In our study, CTC enumeration was performed using the CellSearch® system, the only FDA-cleared platform currently available for CTC detection in solid tumors (15). CTC positivity has been associated with more advanced disease, including higher tumor grade and advanced FIGO stage(13). Therefore, the exclusive inclusion of patients with early-stage cervical cancer in our cohort may account for the absence of detectable CTCs in peripheral blood samples collected before surgery. This observation is consistent with previous reports, as most studies investigating CTCs in cervical cancer have involved patients with locally advanced or metastatic disease(13, 14, 18, 19). Considering the limited sensitivity of peripheral blood sampling for CTC detection in early-stage disease, alternative approaches may be required to improve CTC recovery. Increasing the volume of collected blood samples may represent one potential strategy. In addition, sampling blood from vessels located closer to the primary tumor could enhance CTC detection by increasing the concentration of tumor-derived cells in the analyzed sample(20). Supporting this hypothesis, Francini *et al.* reported, in a pilot study of early-stage endometrial cancer, a higher CTC detection rate in ovarian vein samples compared with peripheral blood (8/10 versus 0/10)(7). Similar observations have been described in colorectal, pancreatic, and lung cancers, where tumor-proximal blood sampling resulted in increased CTC yields compared with peripheral Regarding the surgical management of cervical cancer, updated recommendations were issued in France in 2023 by the French National College of Gynecologists and Obstetricians. These guidelines suggest a sequential approach consisting of initial conization combined with laparoscopic lymph node assessment, followed by delayed hysterectomy through an open abdominal approach 15 to 21 days later. This change in practice was largely influenced by the results reported by Ramirez and Melamed(3, 4), which raised concerns regarding the oncological safety of minimally invasive radical hysterectomy after demonstrating less favorable outcomes compared with open surgery. One proposed explanation for these findings is that minimally invasive procedures may facilitate tumor cell release through mechanical manipulation or pneumoperitoneum-related effects. In our cohort, CTCs were identified only in blood samples collected during the operative procedure (3/11 patients), including one patient after establishment of pneumoperitoneum and two patients before colpotomy. Although based on a limited number of cases, these results suggest that surgical manipulation may influence the transient release of tumor cells into the bloodstream. Similar perioperative increases in CTC detection have been reported during colorectal cancer surgery, supporting the hypothesis that surgical procedures may affect circulating tumor cell dynamics (24, 25).

Given the small size of our cohort, we were not able to determine clinical or pathological factors associated with CTC positivity. Identifying such predictors remains an important objective for future studies, particularly as current evidence in cervical cancer is still limited. In a study including 90 patients with early-stage cervical cancer, Pan *et al.* reported higher baseline CTC levels among patients with FIGO stage II disease, pelvic lymph node involvement, and lymphovascular space invasion(14). Conversely, Du *et al.*, who analyzed 107 patients using immunofluorescence in situ hybridization, did not find any

significant association between CTC counts and clinicopathological characteristics, including age, FIGO stage, tumor differentiation, tumor size, or histological subtype(13).

These findings raise the possibility that CTC assessment may represent a relevant prognostic tool, particularly for identifying patients at increased risk of recurrence. Numerous studies have explored the association between CTC detection and clinical outcomes, including survival and treatment response. In metastatic colorectal cancer, Cohen *et al.* demonstrated that CTC enumeration was an independent predictor of both PFS and OS in a cohort of 430 patients(26). Similarly, De Bono *et al.* reported a significant association between post-treatment CTC levels and OS in patients with metastatic castration-resistant prostate cancer (n = 276)(27). Beyond prognostic assessment, serial CTC monitoring may also provide an opportunity for early evaluation of therapeutic efficacy and treatment adaptation(8, 28, 29). In cervical cancer, Du *et al.* reported that the detection of CTCs (defined as ≥ 1 CTC/3.2 mL of blood, n = 107) was independently associated with poorer outcomes and shorter PFS(13). However, their cohort predominantly included patients with more advanced disease, and the potential impact of surgical intervention on CTC release was not investigated. To date, limited data are available regarding the clinical significance of perioperative CTC detection following tumor resection. In other solid tumors, perioperative CTC dynamics have been associated with oncological outcomes. Sawabata *et al.* showed that, among patients with non-small cell lung cancer who had no detectable CTCs before surgery, postoperative CTC positivity was associated with adverse pathological features, including vascular invasion, lymphatic invasion, and pleural involvement(30). Furthermore, patients with postoperative CTC detection experienced a higher incidence of distant metastases, and the 2-year PFS rate was lower in patients with one detectable CTC compared with those without postoperative CTCs (62.5% versus 94.6%). Similarly, Joose *et al.* demonstrated that prostate biopsy procedures could induce an increase in circulating tumor cell levels, and that this rise was associated with poorer PFS(5).

To our knowledge, this is the first study to report the rate of perioperative CTC detection in patients undergoing surgery for cervical cancer. The presence and count of CTCs during surgery could help to predict the clinical outcome of the patients. Although this hypothesis requires confirmation in larger studies. The main limitation of this study is its low sample size. These preliminary data must be validated in a larger cohort of patients with early-stage cervical cancer and further studies are needed to evaluate the clinical and prognostic value of CTC count and of CTC detection during and after surgical procedures.

Conclusion

This pilot study demonstrates the feasibility of detecting circulating tumor cells (CTCs) in peripheral blood samples collected during surgery for early-stage cervical cancer. Although these findings provide preliminary evidence of intraoperative CTC release, they require confirmation in larger prospective cohorts. Further studies are needed to determine the prognostic significance of perioperative CTC detection and to evaluate its potential role in guiding therapeutic strategies in patients with cervical cancer.

Abbreviations

CC
Cervical Carcinoma
CTC
Circulating tumor cells
PFS
Progression-free survival
OS
overall survival

Declarations

Ethics approval:

this study was conducted in accordance with the ethical principles of the Declaration of Helsinki and applicable national regulations governing clinical research. The study protocol was reviewed and approved by Ethics Committee IDF11 (Ile-de-France XI SAINT-GERMAIN-EN-LAYE), Approval No. 2020-A02456-33), Date: 05/11/2020). The study was registered in a public clinical trials registry (Registration No. NCT04770090, date 25/02/2021).

Consent to participate:

Written informed consent was obtained from all participants prior to their inclusion in the study. All participants were informed about the objectives, procedures, potential risks, and benefits of the research, and their right to withdraw from the study at any time without consequences.

Competiting interests

the authors declare that they have no competing interests.

Funding:

GIRCI SOHO Apithem

Author Contribution

-AJ,MD, SF, GR, CF conception, analysis, drafting of the article- LC, MMD, VM, CM : analysis, drafting of the article- LC, CAP: Conception, conducting tests, analysis, drafting of the articleAll authors read and approved the final manuscript.

Data Availability

The data that support the findings of this study are available from the corresponding author, MD, upon reasonable request.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229–63.
2. Peiretti M, Zapardiel I, Zanagnolo V, Landoni F, Morrow CP, Maggioni A. Management of recurrent cervical cancer: a review of the literature. Surg Oncol Jun. 2012;21(2):e59–66.
3. Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, Ribeiro R, et al. Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer. N Engl J Med. nov 2018;15(20):1895–904.
4. Melamed A, Margul DJ, Chen L, Keating NL, Del Carmen MG, Yang J, et al. Survival after Minimally Invasive Radical Hysterectomy for Early-Stage Cervical Cancer. N Engl J Med. nov 2018;15(20):1905–14.
5. Joosse SA, Beyer B, Gasch C, Nastały P, Kuske A, Isbarn H, et al. Tumor-Associated Release of Prostatic Cells into the Blood after Transrectal Ultrasound-Guided Biopsy in Patients with Histologically Confirmed Prostate Cancer. Clin Chem 1. 2020;66(1):161–8.
6. Wei XQ, Ma Y, Chen Y, Liu X, Zhao M, Zhou LW. Laparoscopic surgery for early cervical squamous cell carcinoma and its effect on the micrometastasis of cancer cells. Med (Baltimore) Aug. 2018;97(34):e11921.
7. Francini S, Duraes M, Rathat G, Macioce V, Mollevi C, Pages L, et al. Circulating Tumor Cell Detection by Liquid Biopsy during Early-Stage Endometrial Cancer Surgery: A Pilot Study. Biomolecules. feb 2023;24(3):428.
8. Bidard FC, Peeters DJ, Fehm T, Nolé F, Gisbert-Criado R, Mavroudis D, et al. Clinical validity of circulating tumour cells in patients with metastatic breast cancer: a pooled analysis of individual patient data. Lancet Oncol apr. 2014;15(4):406–14.
9. Bogani G, Liu MC, Dowdy SC, Cliby WA, Kerr SE, Kalli KR, et al. Detection of circulating tumor cells in high-risk endometrial cancer. Anticancer Res feb. 2015;35(2):683–7.
10. Bidard FC, Jacot W, Kiavue N, Dureau S, Kadi A, Brain E, et al. Efficacy of Circulating Tumor Cell Count-Driven vs Clinician-Driven First-line Therapy Choice in Hormone Receptor-Positive, ERBB2-Negative Metastatic Breast Cancer: The STIC CTC Randomized Clinical Trial. JAMA Oncol 1 jan. 2021;7(1):34–41.
11. Lucci A, Hall CS, Lodhi AK, Bhattacharyya A, Anderson AE, Xiao L, et al. Circulating tumour cells in non-metastatic breast cancer: a prospective study. Lancet Oncol jul. 2012;13(7):688–95.

12. Bork U, Rahbari NN, Schölch S, Reissfelder C, Kahlert C, Büchler MW, et al. Circulating tumour cells and outcome in non-metastatic colorectal cancer: a prospective study. Br J Cancer 14 apr. 2015;112(8):1306–13.
13. Du K, Huang Q, Bu J, Zhou J, Huang Z, Li J. Circulating Tumor Cells Counting Act as a Potential Prognostic Factor in Cervical Cancer. Technol Cancer Res Treat. oct 2020;9:19:1533033820957005.
14. Pan L, Yan G, Chen W, Sun L, Wang J, Yang J. Distribution of circulating tumor cell phenotype in early cervical cancer. Cancer Manag Res. 2019;11:5531–6.
15. Alix-Panabières C, Pantel K. Liquid Biopsy: From Discovery to Clinical Application. Cancer Discov apr. 2021;11(4):858–73.
16. Cibula D, Raspollini MR, Planchamp F, Centeno C, Chargari C, Felix A, Fischerová D, Jahnn-Kuch D, Joly F, Kohler C, Lax S, Lorusso D, Mahantshetty U, Mathevet P, Naik R, Nout RA, Oaknin A, Peccatori F, Persson J, Querleu D, Bernabé SR, Schmid MP, Stepanyan A, Svintsitskyi V, Tamussino K, Zapardiel I, Lindegaard J. ESGO/ESTRO/ESP Guidelines for the management of patients with cervical cancer - Update 2023. Int J Gynecol Cancer. 2023;33(5):649–66. 10.1136/ijgc-2023-004429.
17. Takakura M, Matsumoto T, Nakamura M, Mizumoto Y, Myojyo S, Yamazaki R, et al. Detection of circulating tumor cells in cervical cancer using a conditionally replicative adenovirus targeting telomerase-positive cells. Cancer Sci jan. 2018;109(1):231–40.
18. Wen YF, Cheng TT, Chen XL, Huang WJ, Peng HH, Zhou TC, et al. Elevated circulating tumor cells and squamous cell carcinoma antigen levels predict poor survival for patients with locally advanced cervical cancer treated with radiotherapy. PLoS ONE. 2018;13(10):e0204334.
19. Tewari KS, Sill MW, Monk BJ, Penson RT, Moore DH, Lankes HA, et al. Circulating Tumor Cells In Advanced Cervical Cancer: NRG Oncology-Gynecologic Oncology Group Study 240 (NCT 00803062). Mol Cancer Ther nov. 2020;19(11):2363–70.
20. Pfitzner C, Schröder I, Scheungraber C, Dogan A, Runnebaum IB, Dürst M, et al. Digital-Direct-RT-PCR: a sensitive and specific method for quantification of CTC in patients with cervical carcinoma. Sci Rep 5 feb. 2014;4:3970.
21. Buscail E, Chiche L, Laurent C, Vendrely V, Denost Q, Denis J, et al. Tumor-proximal liquid biopsy to improve diagnostic and prognostic performances of circulating tumor cells. Mol Oncol sep. 2019;13(9):1811–26.
22. Dong J, Zhu D, Tang X, Lu D, Qiu X, Li B, et al. Circulating tumor cells in pulmonary vein and peripheral arterial provide a metric for PD-L1 diagnosis and prognosis of patients with non-small cell lung cancer. PLoS ONE. 2019;14(7):e0220306.
23. Denève E, Riethdorf S, Ramos J, Nocca D, Coffy A, Daurès JP, et al. Capture of viable circulating tumor cells in the liver of colorectal cancer patients. Clin Chem sep. 2013;59(9):1384–92.
24. Wind J, Tuynman JB, Tibbe AGJ, Swennenhuis JF, Richel DJ, van Berge Henegouwen MI, et al. Circulating tumour cells during laparoscopic and open surgery for primary colonic cancer in portal and peripheral blood. Eur J Surg Oncol EJSO 1 sep. 2009;35(9):942–50.

25. Park SY, Choi GS, Park JS, Kim HJ, Ryuk JP, Choi WH. Influence of surgical manipulation and surgical modality on the molecular detection of circulating tumor cells from colorectal cancer. J Korean Surg Soc jun. 2012;82(6):356–64.
26. Cohen SJ, Punt CJA, Iannotti N, Saidman BH, Sabbath KD, Gabrail NY, et al. Relationship of circulating tumor cells to tumor response, progression-free survival, and overall survival in patients with metastatic colorectal cancer. J Clin Oncol Off J Am Soc Clin Oncol 1 jul. 2008;26(19):3213–21.
27. de Bono JS, Scher HI, Montgomery RB, Parker C, Miller MC, Tissing H, et al. Circulating tumor cells predict survival benefit from treatment in metastatic castration-resistant prostate cancer. Clin Cancer Res Off J Am Assoc Cancer Res 1 oct. 2008;14(19):6302–9.
28. Pirozzi G, Tirino V, Camerlingo R, La Rocca A, Martucci N, Scognamiglio G, et al. Prognostic value of cancer stem cells, epithelial-mesenchymal transition and circulating tumor cells in lung cancer. Oncol Rep may. 2013;29(5):1763–8.
29. Pawlikowska P, Faugeroux V, Oulhen M, Aberlenc A, Tayoun T, Pailler E, et al. Circulating tumor cells (CTCs) for the noninvasive monitoring and personalization of non-small cell lung cancer (NSCLC) therapies. J Thorac Dis jan. 2019;11(Suppl 1):S45–56.
30. Sawabata N, Nakamura T, Kawaguchi T, Watanabe T, Ouji NS, Ito T, et al. Circulating tumor cells detected only after surgery for non-small cell lung cancer: is it a predictor of recurrence? J Thorac Dis sep. 2020;12(9):4623–32.

Figures

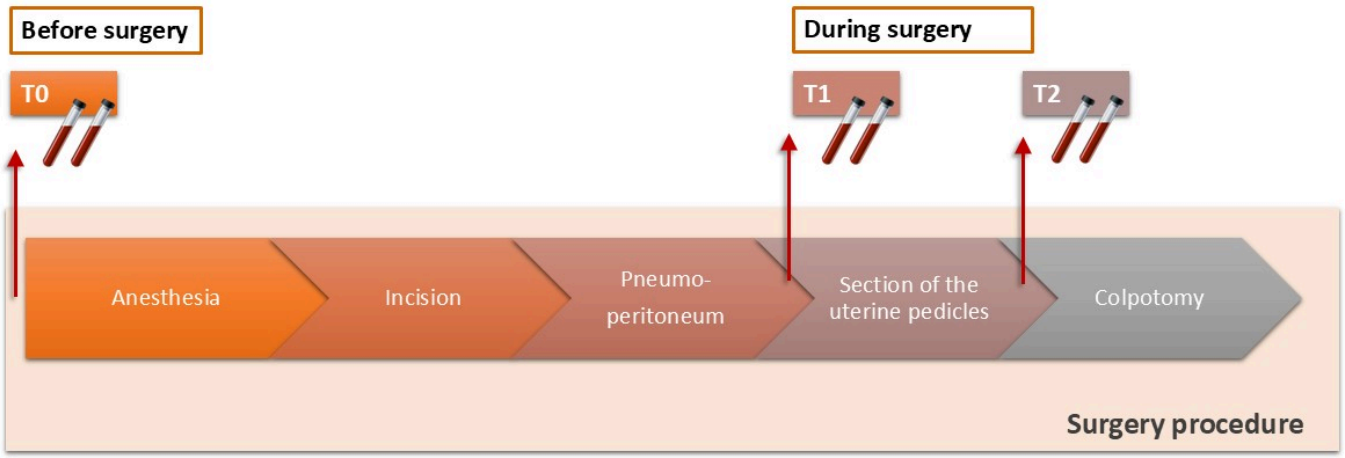


Figure 1

Surgical Procedure of early-stage cervical cancer and timing of blood sample collection. The initial blood sample (T0) was collected from a peripheral vein just before anesthesia and surgery. The other blood samples were obtained during surgery: T1 after creation of pneumoperitoneum and T2 after uterine pedicle coagulation.

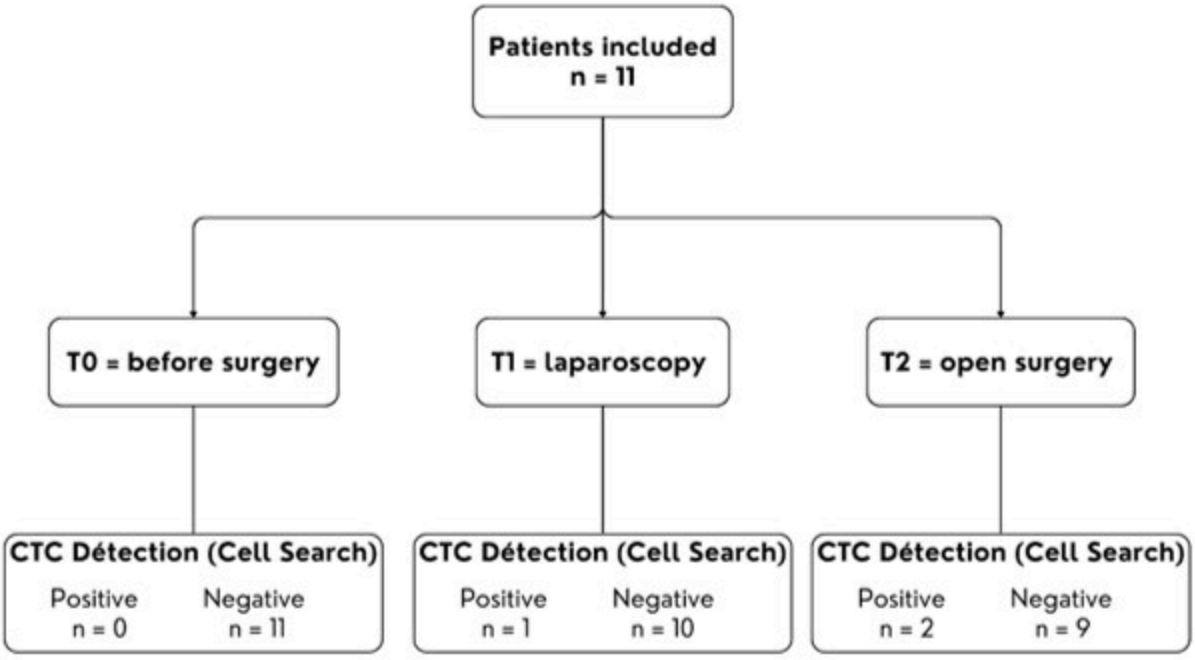


Figure 2

Flow chart showing the number of patients and the results of CTC detection.

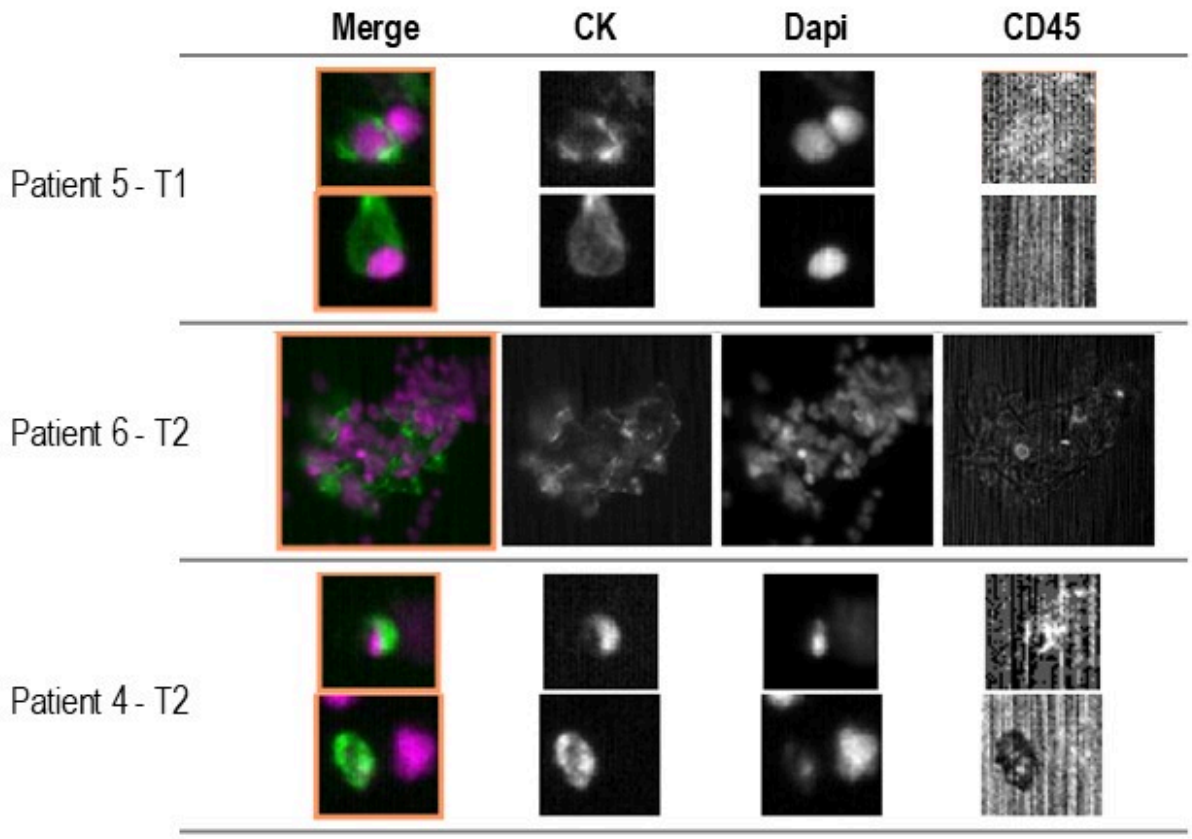


Figure 3

Representative images of circulating cervical cancer cells. This cells were detected with the CellSearch® system in peripheral blood samples from patients with early-stage cervical cancer during surgery.