PATIENT CARE

original reports abstract

Cost Study of the PlasmaJet Surgical Device Versus Conventional Cytoreductive Surgery in Patients With Advanced-Stage Ovarian Cancer

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PURPOSE Adjuvant use of Neutral Argon Plasma (PlasmaJet Surgical Device) during cytoreductive surgery (CRS) for advanced-stage epithelial ovarian cancer improves surgical outcomes. The aim of this study is to examine the costs of adjuvant use of the PlasmaJet during surgery compared with conventional CRS in advanced-stage epithelial ovarian cancer.

MATERIALS AND METHODS The patients were randomly assigned to surgery with or without the PlasmaJet. Analysis of the intra- and extramural health care costs was performed. Costs were divided into three categories: costs of the diagnostic phase (T1), inpatient care up to discharge including costs of surgery (T2), and outpatient care including chemotherapy until 6 weeks after the last cycle of chemotherapy (T3).

RESULTS Overall, 327 patients underwent CRS (surgery with PlasmaJet: n = 157; conventional surgery: n = 170). The mean total health costs were significantly higher for CRS with adjuvant use of PlasmaJet compared with conventional CRS (€19,414 *v* €18,165, $P = .017$). Costs are divided into costs of the diagnostic phase (€2,034 *v* €1,974, $P = .890$), costs of inpatient care (€10,956 *v* €9,556, $P = .003$), and costs of outpatient care (€6,417 *v* €6,628, $P = .147$).

CONCLUSION Mean total health care costs of the use of PlasmaJet in CRS were significantly higher than those for conventional CRS. This difference is fully explained by the additional surgery costs of the use of PlasmaJet. However, surgery with the use of the PlasmaJet leads to a significantly higher percentage of complete CRS and a halving of stomas. A cost-effectiveness analysis will be performed once survival data are available (funded by ZonMw, Trial Register NL62035.078.17).

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INTRODUCTION

Ovarian cancer is the eighth most occurring cancer in women, with, in 2020, almost 314,000 new cases and more than 207,000 deaths worldwide.[1] Conventional treatment for advanced-stage epithelial ovarian cancer (EOC) consists of a combination of chemotherapy and cytoreductive surgery (CRS). Completeness of CRS is the most important independent prognostic factor for survival.[2-5] In recent years, various additional diagnostics and treatment options have been added to the standard policy. One of the additional options during surgery is the possibility to use Neutral Argon Plasma (PlasmaJet Surgical Device of Plasma Surgical, Inc, Roswell, GA), which increases the number of complete cytoreductions.[6] Even previous studies showed that the adjuvant use of the PlasmaJet during CRS for advanced-stage EOC resulted in a significantly higher percentage of complete CRS compared with conventional treatment without the use of the PlasmaJet.[7-10]

The costs of treatment of advanced-stage ovarian cancer can range from €20,000 for only surgery up to €200,000 and even higher for treatment with both surgery and chemotherapy.[11] A study that was performed by an insurance company in the United States estimated the mean cost of care during the first year after diagnosis of ovarian cancer at approximately €55,000.[12] Koole et al[13] performed a cost-effectiveness study in the Netherlands, which focused on the use of hyperthermic intraperitoneal chemotherapy (HIPEC) during surgery for advanced-stage EOC, reporting costs of approximately €70,000, which comprises all costs from diagnosis to recurrent disease. Costs of surgery with the PlasmaJet, however, have not been studied before.

The health care system in the Netherlands is managed by the government and supplemented by nonprofit health insurance companies. All residents are entitled to have a basic insurance package regardless of their income. In addition, employees and the self-employed

ASSOCIATED CONTENT

Appendix

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

What will be the difference in costs in the case of adjuvant use of PlasmaJet during cytoreductive surgery compared with conventional care for advanced-stage ovarian cancer?

Knowledge Generated

The total medical costs in the intervention group were significantly higher than the costs in the control group (€19,414 *v* €18,165; *P* = .017). This significant difference is fully explained by the additional surgery costs of the use of PlasmaJet and not due to an increase in hospitalization or complications.

Relevance

Insight into the extra costs is necessary to be able to weigh them against the social and financial benefits of the adjuvant use of the PlasmaJet in terms of savings through fewer colostomies and an increase in quality of life.

contribute to the Dutch health care costs depending on their company and income.

The Dutch health insurance entitles to free medical treatment in the Netherlands. Care for ovarian cancer including CRS and chemotherapy is fully reimbursed.

The hospitals negotiate individually with the insurers about the rates of their health care products for each year. These health care products consist of a diagnosis-treatment combination. Agreements by the Dutch Healthcare Authority, the rate table for health care products, and other health care products lead to a declaration system and determine the reimbursed costs for specialist medical care in the Netherlands.

When a new product is added to a treatment, the costs are for the hospital unless otherwise has been negotiated with the Dutch Healthcare Authority.

With the current knowledge that surgery with the use of the PlasmaJet improves surgical outcomes and hypothetically leads to longer survival, it is important to determine the increase of operative costs.

The aim of this study is to examine the total medical costs of adjuvant use of the PlasmaJet compared with conventional CRS in patients with advanced-stage EOC.

MATERIALS AND METHODS

Patient Data

A cost analysis was performed in a population of women with advanced-stage EOC, who were included in the PlaComOv study. This multicenter randomized controlled trial in the Netherlands investigated whether the use of the PlasmaJet Surgical Device compared with conventional CRS increased the rate of a successful cytoreduction in women with advanced-stage EOC.[14]

The PlaComOv study was approved by the Medical Ethical Committee of the Erasmus Medical Center, the Netherlands, METC 2017-500, NL62035.078.17, on November 20, 2017.

The study was performed according to the standards outlined in the Declaration of Helsinki. All patients provided written informed consent.

Patients were randomly assigned into two groups: CRS with the use of the PlasmaJet (intervention) or conventional CRS (control). All surgeons (gyneco-oncologists) had experience in performing CRS, and all were trained in the use of the PlasmaJet device in 11 hospitals. In other two hospitals, patients could only be randomly assigned for this study, but no surgery was performed for ovarian cancer.

Inclusion and Exclusion Criteria

Patients with advanced-stage EOC, fallopian tube or peritoneal carcinoma International Federation of Gynecology and Obstetrics (FIGO) stage IIIB-IV who underwent both CRS and chemotherapy, were eligible for inclusion in this cost analysis. The surgical procedure was either primary CRS or interval CRS. Actual inclusion in the study was decided on if advanced-stage EOC (FIGO stage IIIB-IV) was diagnosed before or during surgery. According to the intention-to-treat principle, patients with proven FIGO stage IIIB-IV EOC who underwent surgery with the intention to perform CRS, but in whom surgery was discontinued because of unresectable disease, remained in the study.

Patients with a nonepithelial, borderline ovarian tumor and ovarian metastasis of another primary tumor were excluded.

Diagnostics and Treatment

Diagnostic tests for EOC consisted of physical examination and transvaginal ultrasonography. Furthermore, laboratory research including serum measurement of cancer antigen-125 (CA-125) and carcino-embryonic antigen was achieved, a computed tomography (CT) scan of thorax/abdomen was performed, and, if possible, histologic biopsy was taken.

Patients who met radiologic criteria for nonresectable disease or were diagnosed with FIGO stage IV disease were scheduled for interval CRS and received three courses of

neoadjuvant chemotherapy.[15,16] In the case of radiologic tumor regression or stable disease on a CT scan after three cycles of chemotherapy, patients were eligible for interval CRS.

Diagnostic laparoscopy was performed if the feasibility of surgery was unclear.

The standard chemotherapy regimen consisted of six cycles of carboplatin and paclitaxel with a duration of 3 weeks for each cycle.[5] In primary CRS, all six cycles were given after surgery. In interval CRS, three cycles were given before surgery and three cycles after surgery.

HIPEC was introduced in the Netherlands in 2019.[17] From 2019, all patients age ≤ 75 years with FIGO stage III EOC who underwent interval CRS were eligible to receive an additional HIPEC procedure after complete or optimal CRS.

Cost Calculations

Medical costs from the first appointment at the outpatient clinic up to 6 weeks after the end of the last cycle of chemotherapy as first-line treatment were calculated by multiplying volumes of health care use with the corresponding unit prices. A comparison was made between costs of CRS using the PlasmaJet surgical device versus conventional surgery without the PlasmaJet. Total medical costs consisted of three categories: costs of the diagnostic phase (T1), inpatient care to discharge including costs of surgery (T2), and outpatient care including chemotherapy (T3). A detailed overview of the cost categories is given in Appendix Table A1.

Total costs of surgery using the PlasmaJet and conventional CRS without the PlasmaJet were calculated on the basis of detailed measurement of labor investments, equipment, housing, and overhead. Costs per hour of labor by health care suppliers were estimated on the basis of salary schemes of hospitals. Equipment costs included costs of depreciation and maintenance costs of the PlasmaJet device and were based on an economic life expectancy of 10 years. The cost of a PlasmaJet handpiece is only included if the PlasmaJet has been used during CRS.

Total medical costs per patient consisted of total inpatient and outpatient health care costs. Inpatient care included total costs of surgery using either the PlasmaJet or conventional surgery and costs of care up to hospital discharge, including costs related to a colostomy, diagnostic activities (eg, CT scan and laparoscopy), and postoperative care in the hospital or rehospitalization within 30 days after surgery. Costs of outpatient care included home care and costs of chemotherapy during day treatment. Costs were analyzed from a health care perspective, meaning that societal costs, such as productivity costs, were not taken into account.

Extramural health care use was retrieved from case report forms. Unit prices of the most relevant cost items were determined by following the microcosting method, in which a detailed inventory and measurement of all resources used are made.[18] For instance, duration of surgery was measured to determine costs of health personnel spend on the intervention. Costs of stay at a hospital were determined using the cost manual.[19] A distinction in cost price was made for general and university hospitals. We chose not to invest much time and effort in exploring costs that were unlikely to make any difference to the study results because they were low in price and volume.[20] In the Netherlands, a detailed fee-for-service registration system is used for the reimbursement of medical interventions and diagnostic procedures. Costs were calculated in the European currency (Euro) and corrected for inflation for the year 2020.

Sensitivity Analysis

Since 2019, HIPEC treatment became common practice in patients with FIGO stage III ovarian cancer age ≤ 75 years who undergo interval CRS. Therefore, we performed a sensitivity analysis adding costs of HIPEC to this group, even when HIPEC was not actually applied, to provide a real estimation of current costs of patients with ovarian cancer.

Statistical Analysis

Analyses were performed using an intention-to-treat approach to express the real clinical situation of CRS. Patient characteristics on a categorical level were compared between the intervention and control group using the χ^2 test. Continuous variables were compared using the Mann-Whitney U test. A P value of $< .05$ was considered statistically significant.

The total expenditures were reported as means with standard deviation for the diagnostic phase, inpatient costs, and outpatient costs. Differences in costs between the intervention and control group were compared using the Mann-Whitney U test since costs were not normally distributed. No correction for multiplicity was applied since analyses were of exploratory nature. All analyses were performed using SPSS version 25.

RESULTS

Patients

From February 2018 through September 2020, a total of 383 patients were randomly assigned, 190 to the intervention group and 193 to the control group. All randomly assigned patients had suspected or proven advanced-stage EOC (Fig 1). Overall, 56 patients had to be excluded because they did not meet the inclusion criteria. The clinical characteristics of the 327 included patients in the intention-to-treat analyses are presented in Table 1 and Appendix Table A2.

Forty-five patients (14.8%) underwent primary CRS, and 282 patients (86.2%) interval CRS. A diagnostic laparoscopy was performed in 26 patients (8%) before CRS, in which primary CRS was possible in 12 patients and 14 patients underwent interval CRS.

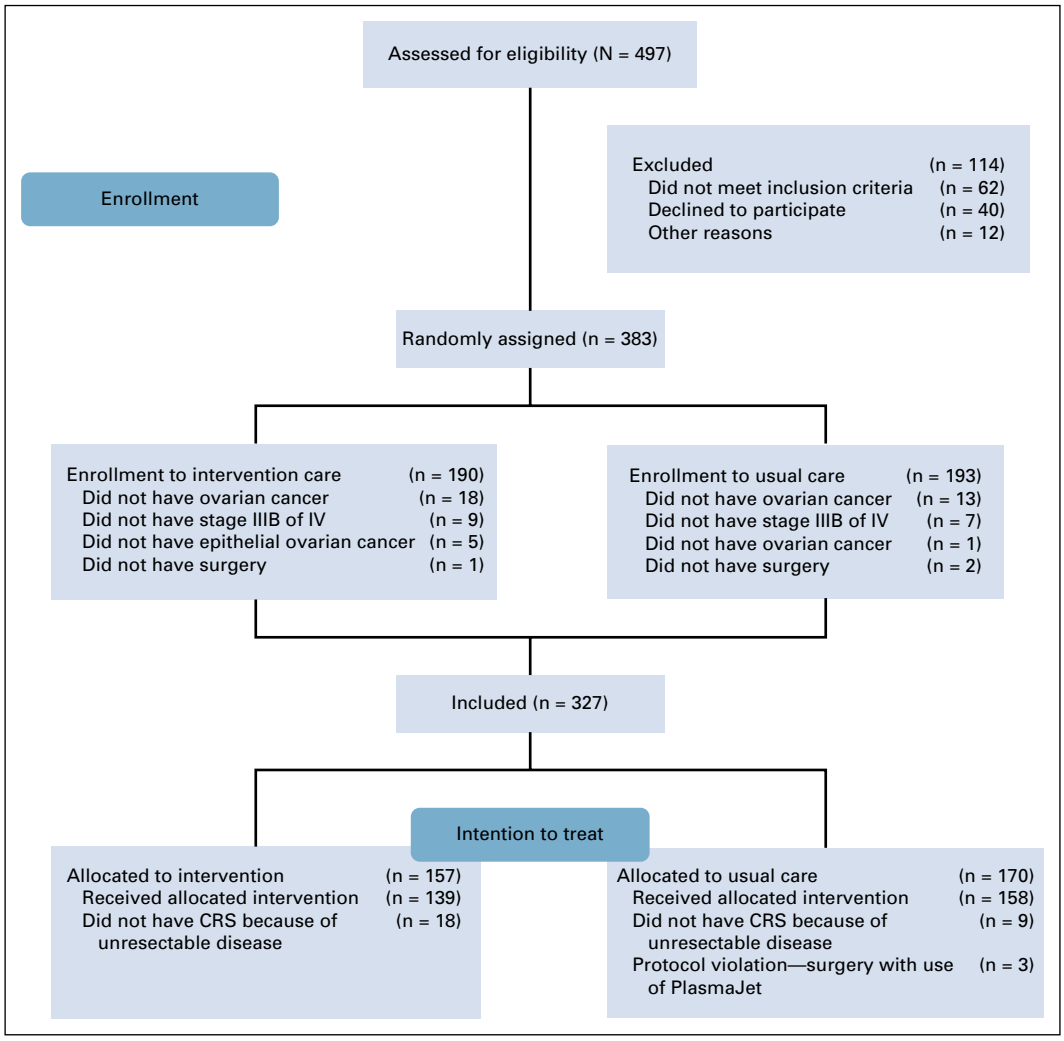

FIG 1. CONSORT flow diagram. CRS, cytoreductive surgery.

Costs

Considering costs of diagnostics (T1), it was found that costs were comparable for the intervention and the control group. Costs of preoperative consultation comprised more than half of total costs of diagnostics, for both the intervention and control group (€995 in both groups).

Costs of surgery (part of T2) were found to be significantly higher for the intervention group (€4,020 *v* €2,951, $P < .001$; Table 2). The higher costs were mainly driven by the cost of the PlasmaJet itself, of which 11 were available in all participating hospitals in the study. Other cost components of surgery were not significantly different between the intervention and control group.

Total costs of inpatient care (T2), including surgery, were found to be higher for the intervention group compared with the control group (€10,956 *v* €9,556, $P = .003$; Table 3).

Costs of outpatient care (T3) were, like costs of diagnostics, not significantly different between the intervention and control group (€6,417 *v* €6.628, $P = .147$). Outpatient costs consisted mainly of costs of chemotherapy.

Comparing total costs of care between patients who underwent surgery with the PlasmaJet and patients who underwent conservative CRS, it was found that costs of care when the PlasmaJet was available during surgery were significantly higher than costs of care when conventional CRS was applied (€19,414 *v* €18,165, $P = .017$).

Sensitivity Analysis

Sensitivity analysis with the inclusion of costs of the HIPEC procedure in patients who met the previously mentioned criteria resulted in total costs of €21,674 for the intervention group versus €20,247 for the control group ($P = .019$; Table 4). The number of additional patients who would receive HIPEC in the hypothetical situation did not differ significantly between the PlasmaJet and the standard CRS group because the age and FIGO stage were equally distributed between the two groups.

TABLE 1. Patient Characteristics

Patient Characteristics	CRS With PlasmaJet (n = 157)	Conventional CRS (n = 170)
Age, years		
Mean (SD)	66.1 (9.6)	65.1 (11.2)
Median (min, max)	67.6 (28.9, 81.3)	65.9 (20.3, 86.1)
WHO performance status, No. (%)		
0	82 (52.2)	90 (52.9)
1	56 (35.7)	53 (31.2)
2	9 (5.7)	8 (4.7)
3	2 (1.3)	5 (2.9)
4	1 (0.6)	0
FIGO stage, No. (%)		
IIIB	11 (7.0)	11 (6.5)
IIIC	96 (61.1)	109 (64.1)
IV	50 (31.8)	50 (29.4)
Primary CRS	20 (12.7)	25 (14.7)
Interval CRS	137 (87.3)	145 (85.3)
HIPEC procedure	29 (18.5)	32 (18.8)

Abbreviations: CRS, cytoreductive surgery; FIGO, International Federation of Gynecology and Obstetrics; HIPEC, hyperthermic intraperitoneal chemotherapy; SD, standard deviation.

DISCUSSION

This study provided a detailed overview of the total medical costs of CRS with the use of the PlasmaJet compared with CRS without the use of the PlasmaJet in patients with advanced-stage EOC.

The total medical costs in the intervention group were significantly higher than the costs in the control group (€19,414 *v* €18,165; $P = .017$). This significant difference is fully explained by the additional surgery costs of the use of PlasmaJet. This includes the one-time purchase of the PlasmaJet, the annual costs for maintenance, and the variable costs of the handpiece that are charged per patient. Costs of the diagnostic phase (T1), inpatient care up to discharge including costs of surgery minus costs of the PlasmaJet (part of T2), and outpatient care including chemotherapy until 6 weeks after the last cycle of chemotherapy (T3) did not differ.

TABLE 2. Detailed Costs of CRS Using the PlasmaJet or Conventional CRS Without the PlasmaJet in Euro's (2020)

Cost Category	CRS With PlasmaJet Mean (95% CI)	Conventional CRS Mean (95% CI)	*P*
Personnel	1,161 (1,036 to 1,268)	1,130 (1,021 to 1,239)	.886
Equipment[a]	908 (873 to 944)	—	< .001*
Housing/ overhead	1,951 (1,783 to 2,118)	1,821 (1,685 to 1,958)	.314
Total costs	4,020 (3,726 to 4,314)	2,951 (2,716 to 3,186)	< .001*

Abbreviation: CRS, cytoreductive surgery.

[a]Equipment consists of costs of the PlasmaJet availability and the use of a PlasmaJet handpiece.

All data in this article were derived from the PlaComOv study. In this study, the patients were randomly assigned to the intervention group (CRS with PlasmaJet) or the control group (conventional CRS without PlasmaJet). If the use of the PlasmaJet is no longer limited to patients randomly assigned to the intervention arm, we suspect that surgeons are likely to use the PlasmaJet in more patients. Therefore, fixed costs of using the PlasmaJet can then be divided among more patients. This will reduce the additional costs per person of surgery using the PlasmaJet.

Whether this difference is also financially significant will depend on a number of things. First, this depends on the number of CRS performed in a hospital. If hospitals can perform other procedures with the PlasmaJet, this will also reduce the fixed costs per procedure and probably, the handpieces can be ordered for an decreased price. Finally, if the hospital bears the extra costs per procedure with the PlasmaJet in addition to the savings from fewer colostomies, the difference will not be financially significant. Most importantly, cost-effectiveness will be calculated in the future to establish the amount of gained disability-adjusted life year.

At the moment, there have been no negotiations with the Dutch Healthcare Authority. This is why the costs of the PlasmaJet will not be reimbursed by health care insurance. In the short term, the cost of this new clinical intervention will be paid by the departments of Gynecologic Oncology, whereas the savings on colostomy care will benefit insurers.

From 2019, halfway through the PlaComOv study, HIPEC was introduced in the Netherlands for patients age ≤ 75 years with FIGO stage III disease undergoing interval CRS. Because random assignment was stratified for the use of HIPEC, the percentage of HIPEC was equally divided between the two groups. Nowadays, all patients age ≤ 75 years with FIGO stage III EOC undergoing interval CRS would be eligible for the HIPEC procedure. The sensitivity analysis showed that the costs in both groups will be higher than the calculated costs from this study.[13,17]

Despite performing a diagnostic laparoscopy in 26 of 327 patients, the number of total futile laparotomies in this study was still 27 (8%). Prevention of performing useless laparotomies could therefore potentially further reduce costs without negatively affecting the quality of life. However, identification of patients eligible for CRS remains a challenge. A Dutch randomized controlled trial previously studied the cost-effectiveness of laparoscopy as a diagnostic tool before primary CRS in ovarian cancer, but found no difference in direct medical costs over a 6-month time horizon although it reduced the number of useless laparotomies.[21] An alternative strategy could be the radiologic selection of patients eligible for CRS. Better predictors in both CT scans and MRIs for complete or optimal

TABLE 3. Average Health Care Use and Costs per Patient in 2020 € for CRS Using the PlasmaJet or Conventional CRS Without the PlasmaJet

	CRS With PlasmaJet (n = 157)		Conventional CRS (n = 170)		
Categories	**Health Care Use Mean (95% CI)**	**Costs**	**Health Care Use Mean (95% CI)**	**Costs**	***P***
Diagnostics					
Preoperative vulnerability analysis	0.3 (0.2 to 0.4)	123 (74 to 171)	0.3 (0.2 to 0.4)	144 (92 to 199)	.865
Preoperative intake[a]	3.0 (3.0 to 3.0)	995 (995 to 995)	3.0 (3.0 to 3.0)	995 (995 to 995)	-
Diagnostic laparoscopy	0.1 (0.1 to 0.2)	386 (197 to 590)	0.1 (0.0 to 0.1)	249 (115 to 390)	.396
Diagnostic laparotomy	0.0 (0 to 0)	58 (-15 to 94)	0.0 (0.0 to 0.1)	107 (22 to 194)	.372
X-ray of thorax	0.0 (0 to 0)	1 (0 to 2)	0.0 (0 to 0)	1 (1 to 2)	.936
CT scan	1.1 (1.0 to 1.1)	172 (164 to 177)	1.1 (1.1 to 1.2)	179 (171 to 188)	.206
MRI	0.0 (0.0 to 0.1)	9 (2 to 17)	0.0 (0.0 to 0.1)	10 (3 to 18)	.891
Echo	0.7 (0.6 to 0.8)	63 (56 to 69)	0.6 (0.6 to 0.7)	59 (52 to 66)	.372
Other preoperative diagnostic scan[b]	2.1 (2.0 to 2.3)	228 (178 to 282)	2.3 (2.1 to 2.4)	230 (180 to 281)	.985
Total diagnostics	—	2,034 (1,825 to 2,255)	—	1,974 (1,802 to 2,152)	.890
Inpatient care					
Surgery	—	4,020 (3,726 to 4,314)	—	2,951 (2,716 to 3,186)	< .001*
Hospital days in PACU	0.2 (0.1 to 0.3)	259 (159 to 370)	0.2 (0.1 to 0.3)	263 (169 to 363)	.814
Hospital days in ICU	0.4 (0.2 to 0.6)	917 (506 to 1,335)	0.4 (0.3 to 0.5)	821 (563 to 1,099)	.721
Hospital days in ward	7.4 (6.6 to 8.3)	4,058 (3,547 to 4,550)	7.1 (6.2 to 8.0)	3,958 (3,364 to 4,594)	.410
HIPEC	0.2 (0.1 to 0.2)	905 (589 to 1,193)	0.2 (0.1 to 0.2)	922 (639 to 1,227)	
In-hospital scans	0.6 (0.5 to 0.8)	58 (45 to 73)	0.5 (0.4 to 0.6)	52 (38 to 66)	.537
Relaparotomy	0.1 (0 to 0.1)	154 (50 to 265)	0.0 (0 to 0)	53 (-7 to 115)	.096
Rehospitalization days in ward	1.0 (0.4 to 1.7)	548 (185 to 919)	0.9 (-0.1 to 1.9)	486 (-14 to 998)	.409
Rehospitalization for scans	0.3 (0.2 to 0.4)	34 (22 to 46)	0.2 (0.1 to 0.3)	25 (12 to 38)	.026*
Total inpatient care	—	10,956 (9,817 to 12,176)	—	9,556 (8,401 to 10,712)	.003*
Outpatient care					
Stoma	0.1 (0 to 0.1)	179 (66 to 300)	0.1 (0.1 to 0.2)	368 (217 to 527)	.056
Chemotherapy	6.0 (6.0 to 6.0)	6,150 (6,150 to 6,150)	6.0 (6.0 to 6.0)	6,150 (6,150 to 6,150)	—
Homecare hours	1.4 (0.9 to 1.9)	87 (56 to 122)	1.8 (1.0 to 2.5)	110 (64 to 160)	.769
Total outpatient care	—	6,417 (6,292 to 6,552)	—	6,628 (6,461 to 6,801)	.147
Total costs	—	19,414 (18,161 to 20,668)	—	18,165 (16,920 to 19,409)	.017*

Abbreviations: CA-125, cancer antigen-125; CEA, carcino-embryonic antigen; CRS, cytoreductive surgery; CT, computed tomography; HIPEC, hyperthermic intraperitoneal chemotherapy; ICU, intensive care unit; PACU, post-anesthesia care unit.

[a]Includes consults with gynecologist, medical-oncologist, and anesthesiologist.

[b]Includes CA-125, CEA, PET-CT, histologic puncture (ultrasound-guided), histologic puncture (CT-guided), cytologic puncture (ultrasound-guided), colonoscopy, CR-BOZ, cytologic ascites, EBUS, echo biopsy, gastroscopy, histology, pleural puncture, transesophageal ultrasound, and pathologic tests.

TABLE 4. No. of Patients With HIPEC Treatments and Total Costs (2020 €) for Sensitivity Analysis

HIPEC,[a]	**CRS With PlasmaJet**	**Conventional CRS**	***P***
No. (%)	50 (32%)	49 (29%)	.552
Total cost including additional HIPEC mean (95% CI)	21,674 (20,338 to 23,009)	20,247 (18,885 to 21,609)	.019*

NOTE. HIPEC treatment was added to the total costs for all patients age < 76 years with stage III ovarian cancer who underwent interval CRS and who had not had HIPEC in their actual treatment.

Abbreviations: CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy.

[a]Includes both patients who actually received HIPEC treatment and patients who would receive HIPEC treatment with current treatment protocols.

CRS would reduce costs. To date, no effective imaging strategies are available that offer effective prevention against futile laparotomies.

Gynecologist-oncologists and other surgeons should be trained to use the PlasmaJet. One day of training is required to use the PlasmaJet. The costs of this training during our study were paid from the subsidy awarded to the PlaComOv study and have not been included in this cost calculation. It seems obvious that the one-off costs of a training will be part of the purchase of the PlasmaJet.

A limitation of this study is that the indirect costs because of productivity losses and informal caregiver costs are not included in the analysis. The median age at diagnosis was 67 years and was equally distributed among both groups. The percentage of women under age 67 years who were employed at diagnosis and experienced loss of productivity is unknown.

To determine whether the costs will turn out differently in the long term, a study should be performed with a longer follow-up period. In that study, costs of poly(adenosine diphosphate-ribose) polymerase inhibitors, which are currently prescribed as maintenance therapy at the end of primary treatment, should be added.[22]

Costs for molecular diagnostics on the tumor tissue and for genetic research should also be included in a study with a longer follow-up period.[23,24] These tests on tumor tissue could not be claimed from the insurer at the time of our study. Because the costs would be the same for both groups, this does not influence the outcome of this study.

Finally, in a long-term analysis, the difference in progression-free and overall survival between the two study groups will become clear.

In conclusion, the mean total health care costs of using PlasmaJet during CRS (€19,414) were significantly higher than those for conventional CRS (€18,165) in advanced-stage EOC. This study showed a difference in costs between the two groups of €1,249, which only consists of the additional costs of the PlasmaJet and was not due to an increased demand for care because of complications or a longer hospitalization. In authors' opinion, the benefits of implementing the PlasmaJet outweigh the increase of these costs. The PlasmaJet is promising with a greater chance of complete CRS.

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DISCLAIMER

Neither ZonMw nor Plasma Surgical were involved in the study design; the collection, analysis, or interpretation of data; nor in the writing of this manuscripts or in the decision to submit this manuscript for publication.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al: Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71:209-249, 2021
2. Colombo N, Sessa C, Bois AD, et al: ESMO-ESGO consensus conference recommendations on ovarian cancer: Pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. Int J Gynecol Cancer, 2019
3. du Bois A, Reuss A, Pujade-Lauraine E, et al: Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: A combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: By the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO). Cancer 115:1234-1244, 2009
4. Landrum LM, Java J, Mathews CA, et al: Prognostic factors for stage III epithelial ovarian cancer treated with intraperitoneal chemotherapy: A Gynecologic Oncology Group study. Gynecol Oncol 130:12-18, 2013
5. Vergote I, Tropé CG, Amant F, et al: Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med 363:943-953, 2010
6. Nieuwenhuyzen-de Boer GM, Hofhuis W, Reesink-Peters N, et al: Adjuvant use of PlasmaJet device during cytoreductive surgery for advanced-stage ovarian cancer: Results of the PlaComOv-study, a randomized controlled trial in the Netherlands. Ann Surg Oncol 29:4833-4843, 2022
7. Nieuwenhuyzen-de Boer GM, van der Kooy J, van Beekhuizen HJ: Effectiveness and safety of the PlasmaJet® device in advanced stage ovarian carcinoma: A systematic review. J Ovarian Res 12:71, 2019
8. Prodromidou A, Pandraklakis A, Iavazzo C: The emerging role of neutral argon plasma (PlasmaJet) in the treatment of advanced stage ovarian cancer: A systematic review. Surg Innov 27:299-306, 2020
9. Volcke A, Van Nieuwenhuysen E, Han S, et al: Experience with PlasmaJet in debulking surgery in 87 patients with advanced-stage ovarian cancer. J Surg Oncol 123:1109-1114, 2021
10. Manning-Geist BL, Hicks-Courant K, Gockley AA, et al: A novel classification of residual disease after interval debulking surgery for advanced-stage ovarian cancer to better distinguish oncologic outcome. Am J Obstet Gynecol 221:326 e1-e7, 2019
11. Ovarian Cancer Treatment Cost: Costhelper Health, 2021. https://health.costhelper.com/ovarian-cancer.html
12. Urban RR, He H, Alfonso-Cristancho R, et al: The cost of initial care for medicare patients with advanced ovarian cancer. J Natl Compr Canc Netw 14:429-437, 2016
13. Koole SN, van Lieshout C, van Driel WJ, et al: Cost effectiveness of interval cytoreductive surgery with hyperthermic intraperitoneal chemotherapy in stage III ovarian cancer on the basis of a randomized phase III trial. J Clin Oncol 37:2041-2050, 2019
14. Nieuwenhuyzen-de Boer GM, Hofhuis W, Reesink-Peters N, et al: Evaluation of effectiveness of the PlasmaJet surgical device in the treatment of advanced stage ovarian cancer (PlaComOv-study): Study protocol of a randomized controlled trial in the Netherlands. BMC Cancer 19:58, 2019
15. Borley J, Wilhelm-Benartzi C, Yazbek J, et al: Radiological predictors of cytoreductive outcomes in patients with advanced ovarian cancer. BJOG 122:843-849, 2015
16. Forstner R, Sala E, Kinkel K, et al: ESUR guidelines: Ovarian cancer staging and follow-up. Eur Radiol 20:2773-2780, 2010
17. van Driel WJ, Koole SN, Sonke GS: Hyperthermic intraperitoneal chemotherapy in ovarian cancer. N Engl J Med 378:1363-1364, 2018
18. Gold MR, Siegel JE, Russel LB, et al: Cost-effectiveness in Health and Medicine. New York, NY, Oxford University Press, 1996
19. Hakkaart-van Roijen L, van der Linden N, Bouwmans C, et al: Kostenhandleiding: Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg, 2015
20. Drummond MF, MJ Sculpher, Claxton GK, et al: Methods for the Economic Evaluation of Health Care Programmes. New York, NY, Oxford University Press, 2005
21. van de Vrie R, van Meurs HS, Rutten MJ, et al: Cost-effectiveness of laparoscopy as diagnostic tool before primary cytoreductive surgery in ovarian cancer. Gynecol Oncol 146:449-456, 2017
22. Harrison RF, Fu S, Sun CC, et al: Patient cost sharing during poly(adenosine diphosphate-ribose) polymerase inhibitor treatment in ovarian cancer. Am J Obstet Gynecol 225:68.e1-e11, 2021
23. Bekos C, Grimm C, Kranawetter M, et al: Reliability of tumor testing compared to germline testing for detecting BRCA1 and BRCA2 mutations in patients with epithelial ovarian cancer. J Pers Med 11:593, 2021
24. Moschetta M, George A, Kaye SB, Banerjee S: BRCA somatic mutations and epigenetic BRCA modifications in serous ovarian cancer. Ann Oncol 27:1449-1455, 2016

APPENDIX

TABLE A1. Overview of Cost Prices in 2020 €[19]

Item	Unit	Price
Preoperative consult (eg, geriatrician, cardiologist, etc)	Consult	€461
Consult gynecologist	Consult	€461
Consult oncologist	Consult	€461
Preoperative consult anesthesiologist	Consult	€74
Laboratory tests (diagnostic)	Test	€12
CA-125	Test	€13
CEA	Test	€8
Ultrasound	Scan	€92
CT scan of thorax-abdomen	Scan	€159
MRI scan of abdomen	Scan	€244
PET-CT	Scan	€1,138
X-ray of thorax	Scan	€65
X-ray of abdomen	Scan	€46
Transesophageal ultrasound	Scan	€865
Cystogram	Scan	€183
Electrocardiogram	Scan	€384
Pyelogram	Scan	€169
Histologic puncture—CT	Puncture	€654
Histologic puncture—ultrasound	Puncture	€136
Cytologic ascites/abscess puncture—ultrasound	Puncture	€206
Cytologic pleural puncture—ultrasound	Puncture	€289
Colonoscopy	Scopy	€267
Gastroscopy	Scopy	€263
Ultrasound-bronchoscopy	Scopy	€783
Pathologic examination	Test	€129
Laparoscopy	Treatment	€3,028
Laparotomy	Treatment	€3,028
Relaparotomy	Treatment	€3,028
HIPEC	Treatment	€4,900
Packed cells	Pack	€238
Platelets	Pack	€574
Fresh frozen plasma	Pack	€205
Stay in the postanesthesia care unit	Day	€1,313
Stay in the intensive care unit	Day	€2,216
Stay in hospital ward (academic)	Day	€706
Stay in hospital ward (general)	Day	€487
Chemotherapy per cycle	Treatment	€1,025
Parenteral nutrition	Day	€289
Enteral nutrition (fixed)	Stay	€67
Enteral nutrition (variable)	Day	€25

Abbreviations: CA-125, cancer antigen-125; CEA, carcinoembryonic antigen; CT, computed tomography; HIPEC, hyperthermic intraperitoneal chemotherapy; MRI, magnetic resonance imaging; PET-CT, positron emission tomography and computed tomography.

TABLE A2. Outcome of Inpatient Care (for cost calculation T2) of Patients Who Underwent CRS With PlasmaJet Compared With Conventional CRS Without PlasmaJet

Categories of Inpatient Care	CRS With PlasmaJet (n = 157)	Conventional CRS (n = 170)	*P*
Operative time, minutes			
Mean (SD)	236 (126)	222 (110)	.326
Median (min, max)	210 (29, 671)	194 (48, 595)	
Missing, No. (%)	6 (3.8)	4 (2.4)	
Transfusion during surgery, No. (%)	41 (26.1)	45 (26.5)	.877
Colostomy, No. (%)	9 (5.7)	20 (11.8)	.092
Intensive care postoperative, No. (%)	34 (21.7)	40 (23.5)	.785
Intensive care, days			
Mean (SD)	1.9 (1.9)	1.6 (0.9)	.339
Median (min, max)	1.0 (1, 11)	1.0 (1, 5)	
Hospitalization, days			
Mean (SD)	8.7 (6.5)	7.9 (6.4)	.221
Median (min, max)	6.5 (2, 35)	6.0 (2, 51)	
Missing, No. (%)	3 (1.9)	0	
Discharge, No. (%)			
Home without nursing care	100 (63.7)	110 (64.7)	.955
Home with nursing care	34 (21.7)	39 (22.9)	
Nursing home	4 (2.5)	3 (1.8)	
Rehabilitation center	2 (1.3)	2 (1.2)	
Hotel providing nursing care	9 (5.7)	12 (7.1)	
Hospice	1 (0.6)	0	
Death	0	1 (0.6)	

Abbreviations: CRS, cytoreductive surgery; SD, standard deviation.