

## Role Guided Intraperitoneal Port-A-Cath Insertion in The Management of Cancer Ovary of Fluoroscopic

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### Abstract

#### Introduction :

The use of intraperitoneal (IP) chemotherapy as a treatment for ovarian cancer has been demonstrated to result in improved survival.

**Aim of the work:** The aim of this work is to evaluate the applicability and efficacy of fluoroscopic placed intraperitoneal port-A-cath and to assess the response rate to intraperitoneal chemotherapy in cases of ovarian carcinoma .

**Methods:** The studied group included ,22 female patients with malignant ovarian cancer whom referred from gynecological surgery and gynecological oncology units to the Vascular and Interventional Radiology Unit, Ain Shams University Hospitals, for peritoneal port-A-cath application. All the patients were known cases of either primary or recurrent ovarian cancer , underwent cytoreductive surgery and referred to us .

**Results:** Intraperitoneal port-A-cath with the aid of fluoroscopy showed highest technical success ( 91.9% ) and lowest complication rate on the long run compared to other methods of peritoneal access .

Patients with cancer ovary showed significant improvement of the disease process denoted by changes in the degree of ascites , peritoneal nodules and tumor marker level after receiving combined IV/ IP chemotherapy.

**Conclusion:** Port catheters proved to be the most safe method of long term access to the peritoneal cavity with the lowest complication rate compared to other methods of access to the peritoneal cavity.

**Key words:** port-a-cath.,ovarian cancer,fluoroscopy,intraperitoneal chemotherapy.

### INTRODUCTION

Ovarian cancer is the most common cause of death among women who develop gynecological malignancies (1).

The high mortality rate is attributed to the fact that >75 % of the patients are diagnosed at an advanced stage of the disease (1).

The initial lines of treatment with ovarian carcinoma include cytoreductive surgery with tumor debulking whenever possible to the greatest possible extent with the remaining amount of the disease after surgery (2).

Intravenous (IV) combination chemotherapy became the standard postoperative treatment regimen for women with advanced-stage ovarian cancer . (3).

The characteristic feature of ovarian cancer specially epithelial ovarian cancer (EOC) being chemo sensitive and the intraperitoneal spread of disease even in the early stages have enhanced the strategy of locoregional management with delivery of the chemotherapeutic agent directly into the peritoneal cavity.This resulted in reduction of the systemic effects and furthermore concentrating the drug to the tumor site many

times higher than it would have been tolerated through the systemic circulation .(4)

The Gynecologic Oncology Group (GOG) have demonstrated the superiority of combination IV/IP therapy compared to IV chemotherapy alone (1).

Women proved to have adenocarcinoma by biopsy or cytology with stage III/ IV (pleural effusions only) epithelial ovarian, fallopian tube or primary peritoneal carcinoma if optimally debulked they receive IV paclitaxel 175mg/m<sup>2</sup> and IP carboplatin 5 (day 1) and IP paclitaxel 60mg/m<sup>2</sup> (day 8) q28 days×6 cycles .(1)

An effective and safe method for delivery of the chemotherapeutic agent into the peritoneal cavity is recently achieved by the placement of intraperitoneal port-A-cath under fluoroscopy guidance .(5)

#### THE AIM OF THE WORK

The aim of this work is to evaluate the applicability and efficacy of fluoroscopic placed intraperitoneal port-A-cath and to assess the response rate to intraperitoneal chemotherapy in cases of ovarian carcinoma .

**METHODS**

From September 2010 to April 2012, Twenty two female patients with age ranging from 40 to 72 years old (with mean age = 54.5 years) suffering from malignant ovarian carcinoma were referred from gynecological surgery and gynecological oncology units to the vascular and Interventional Radiology Unit, Ain - Shams University Hospitals, for peritoneal port-A-cath application.

In our study, the inclusion and exclusion criteria were as follows, we included patients with Stage III ovarian carcinoma, Stage IV ovarian carcinoma (associated with pleural effusion only), tumor recurrence, minimal adhesions, tumor in other stages resistant to traditional chemotherapy regimens, attempt to control malignant ascites, unless massive, must be partially drained first.

We excluded patients suffering from stage IV (distant spread except those with pleural effusion only), massive peritoneal adhesions, previous pelvic irradiation, tense ascites unless drained, patients with high bleeding profile liable for uncontrollable hemorrhage unless corrected (INR > 1.6 and platelet count less than 70000), those with very poor general condition, peritoneal sepsis or marked comorbidity were excluded as well.

The treatment decision was made after multidisciplinary discussion between surgeons, oncologist and radiologists on the basis of clinical, laboratory and radiological criteria confirming proper staging and as base line data for follow up comparison .

The patients or their legal representatives were given detailed information on the details of the procedure. A written consent was taken from the patients; in which the risks of the procedure.

Sonography was performed before the surgical preparation to localize an area in the abdomen in which there was a large pocket of ascites and to exclude loculations . At least a moderate amount of ascites should be present at the time of port placement to help insure placement of the catheter in an optimal location.

The ascites grade was assessed in terms no improvement (stationary), improvement with scores according to the degree of improvement or deteriorated after receiving peritoneal chemotherapy.

The port site was chosen over a bone to allow for easy needle access. Usually the site was over the inferior aspect of the lower ribs in the anterior midclavicular line.

Prophylactic pre-procedural antibiotic coverage for skin flora with intravenous cefazolin & metronidazole was administered .

As for technical steps , Ultrasonography was used to mark the puncture site of large-volume ascites without loculations then 18G Chiba needle was used for ultrasound (US)-guided puncture. Local anesthesia with xylocaine before the puncture. After the stylet of the needle was removed, A 0.035-in. guidewire (Amplatz Super Stiff; Boston Scientific, USA) was advanced into the pelvic aspect of the peritoneal cavity under fluoroscopy and a 6F dilator was inserted over the guidewire, then the guidewire was removed and the dilator was capped. The port pocket was created above the puncture site over the anterolateral lower ribs. Skin and subcutaneous tissues were infiltrated with local anesthetic. A 3–4-cm incision was made and a subcutaneous pocket was prepared according to the reservoir size. A subcutaneous tunnel was created between the pocket and the ascites entry point with a tunneler after local anesthesia. The reservoir end of the catheter was connected to the tunneler, pulled through the tunnel, cut to the appropriate length, and connected to the reservoir .The reservoir was placed into the pocket and fixed to skin with a 19G Huber needle. Then the guidewire was again advanced to the pelvic portion of the peritoneal cavity through the dilator under fluoroscopy guidance and serial dilatation was performed. A 16F peel-away sheath was placed over the guidewire and the catheter was advanced through the peel-away sheath into the ascites; the peel-away sheath was then removed. Port-catheter function and integrity was confirmed with sterile saline injection and ascites aspiration via the Huber needle.

The port-catheter position along its course was confirmed with fluoroscopy , then the port site was closed with two layers of subcutaneous 3-0 Vicryl absorbable sutures. In patients with a large amount of subcutaneous fat tissue, 3-0 nonabsorbable sutures were used to prevent possible leakage. The ascites entry site was closed with 3-0 nonabsorbable sutures.

Large-volume paracentesis was performed immediately after skin closure.

**RESULTS**

In our study a 90.9 % technical success rate was achieved with adequate positioning of the reservoir in a quiet well designed pocket and the distal end of the intraperitoneal catheter tip in the peritoneal cavity . Patency of the catheter was confirmed. Some of the patient confirmed efficient placement of the port and absence of adhesions by injection of low dose of diluted water soluble contrast media in to the port to ensure good smearing of the peritoneal reflections.

In our study clinical success as regarding the response to chemotherapy was defined as improvement in tumor marker after receiving combined IV / IP chemotherapy, reduction in the grade/size of ascites and peritoneal nodules if present before therapy. The later two judging points are well demonstrated on follow up by pelvi abdominal CT . In our study, 68.5 % (15 patients) of the patients responded to peritoneal chemotherapy, 18 % (4 patients) was stationary and only 13.5 % (3 patients) of the patients deteriorated.

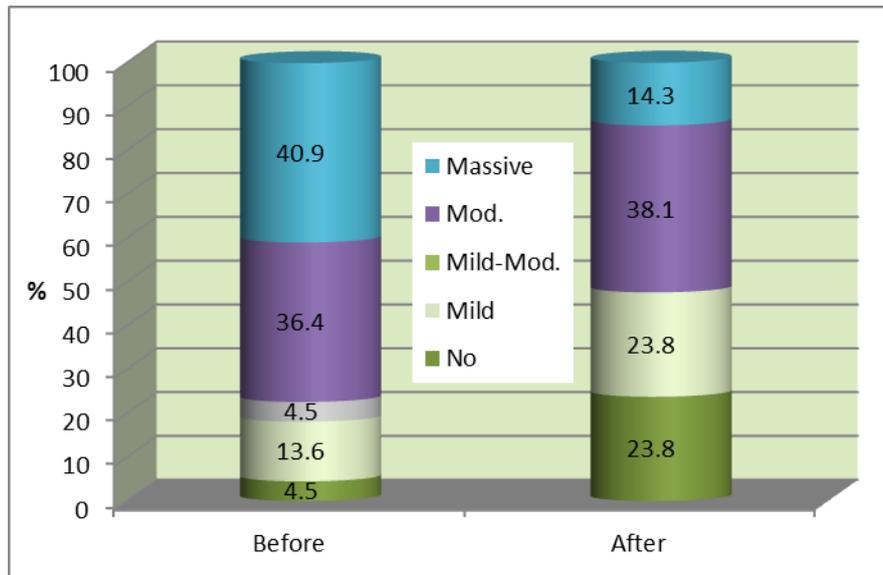
In our study 4 patient developed port related complications (18.2%) as adhesive intestinal obstruction, skin infection , malpositioned and blocked port-A-cath & 5 patients developed peritoneal chemotherapy related complications (22.7%) which was mainly GIT upset and neutropenia .

Two patients died and the reason was not known so they weren't assessed in the results.

Regarding change of degree of ascites before and after peritoneal chemotherapy , It was found that 6 patients were stationary, 15 patients improved with different degrees where (changing one degree i.e. from moderate to mild or from severe to moderate takes score 1 ,and change from marked to mild or moderate to no ascites takes score 2 and finally change from marked to no ascites takes score 3 ).In our study the 15 patients that improved are as follows where 6 patients responded with score 1, 6 other patients responded with score 2 and 3 patients responded with score 3 and finally only 1 patient deteriorated.

**Table (1):Comparison of the pre and post procedure ascites degree in pelviabdominal CT**

					Total
			After	Before	
CT ASCITES	No	Count %	5 23.8%	1 4.5%	6 14.0%
	Mild	Count %	5 23.8%	3 13.6%	8 18.6%
	Mild to moderate	Count %	0 0.0%	1 4.5%	1 2.3%
	Moderate	Count %	8 38.1%	8 36.4%	16 37.2%
	Massive	Count %	3 14.3%	9 40.9%	12 27.9%
Total		Count %	21 100.0%	22 100.0%	43 100.0%

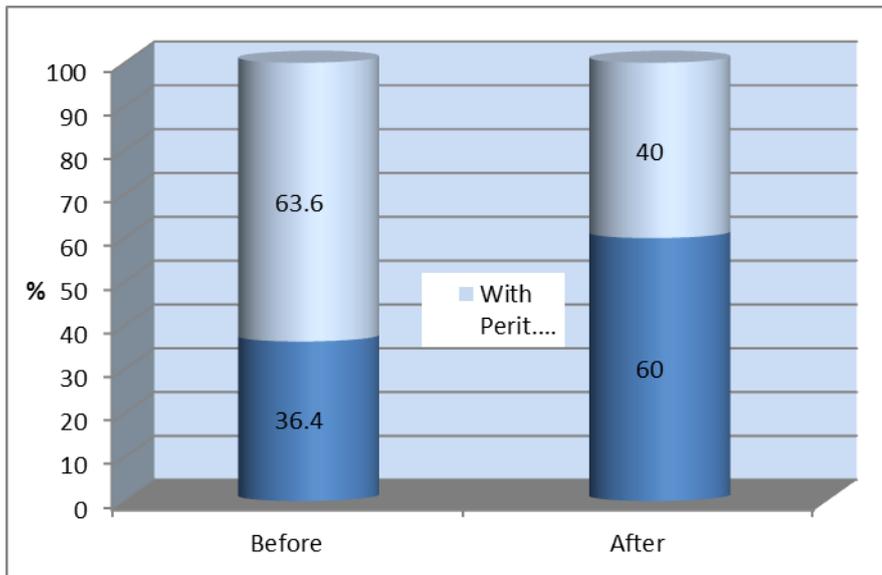


**Fig.(1):Illustrative diagram showing comparison of the pre and post procedure ascites grade in pelviabdominal**

The peritoneal nodules were assessed in terms no improvement (stationary) or improvement or deteriorated after receiving peritoneal chemotherapy. It was found that 10 patients were stationary, 10 patients improved and only 2 patients deteriorated.

**Table (2): Comparison of the pre and post procedure peritoneal nodules assessment in Pelviabdominal CT**

				After	Before	Total
	Peritoneal Deposit	-ve	Count	12	8	20
			%	60.0%	36.4%	47.6%
		+ve	Count	8	14	22
			%	40.0%	63.6%	52.4%
	Total		Count	20	22	42
			%	100.0%	100.0%	100.0%

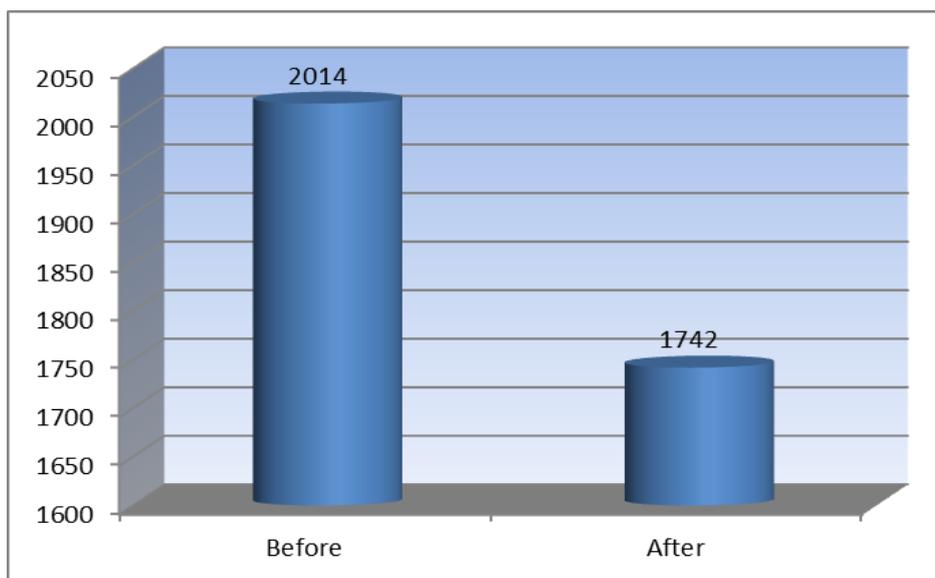


**Fig. (2): Illustrative diagram showing pre and post procedure peritoneal deposit in pelviabdominal CT**

The tumor marker was assessed in terms of either improvement or deteriorated. It was found that 15 patients had an improving tumor marker level with peritoneal chemotherapy while 7 patients deteriorated .

**Table (3): Showing change in the tumor marker level before and after treatment**

Descriptive Statistics:			
		Tumor marker Before peritoneal chemotherapy.	Tumor marker after peritoneal chemotherapy .
N		22	20
Median		1953.5	940
Minimum		802	112
Maximum		4780	4900
Percentiles	25	1235	492.5
	75	2792.5	3337.5



**Fig.(3):Showing illustrative diagram representing the mean tumor marker level before and after peritoneal chemotherapy**

## Discussion

Level I evidence and a National Cancer Institute (NCI) consensus statement support the use of intraperitoneal (IP) chemotherapy to improve survival in patients with optimally resected epithelial ovarian cancer (6). Three randomized phase III trials performed by the Gynecologic Oncology Group (GOG) have demonstrated the superiority of combination IV/IP therapy compared to IV chemotherapy alone (6).

The low incidence of complications with simple intravenous drug delivery most likely accounts for its more common utilization (6). However, in some specific situations, intraperitoneal drug delivery, or intraperitoneal drug delivery combined with intravenous drug delivery have been definitely shown to improve outcome (6).

Complications reported in our study either to be peritoneal port related as a kinked catheter, blocked catheter, leakage of infusate, peritonitis, or abscess, bowel injury, gastrointestinal necrosis and perforation & some pain and discomfort or peritoneal chemotherapy related as delayed nausea, nephrotoxicity, hypersensitivity reactions, abdominal pain & neurotoxicity.

Port complications can be kept to a minimum with careful technique, but they are still not completely avoidable. Although infection may theoretically be reduced by the avoidance of placement during grossly contaminated surgeries, but there is no proven method of preventing the adhesions that cause obstruction to flow.

In our study with a radiologically placed peritoneal port-catheter as an effective alternative method for intraperitoneal approach. Portcatheters were successfully placed under ultrasonographic and fluoroscopic guidance.

In our study the main technical obstacle was peritoneal adhesions which occurred in two patients from the 22 patients. Savin et al, (7) reported one patient (4%) that had clinical failure. He had his port placed the day after paracentesis and loculated ascites was not recognized at the time of placement, likely because of the presence of only minimal residual ascites at the time of port placement.

In our study 4 patient developed complications (18.2 %), 1 of them was serious and life endangering, while the others just required port removal. The serious complication was adhesive intestinal

obstruction which required surgical interference with adhesiolysis of the peritoneal adhesions, one patient developed skin infection related to the port reservoir site along the costal margin, another patient developed malpositioned catheter and the last patient developed port blockage. The later 3 required port removal and antibiotic coverage. Savin et al.(7) reported a series of 24 patients where Four patients (17%) developed bacterial peritonitis, three of them responded to antibiotics, and one had to have his catheter removed. Rosenblum et al. (9) detected three cases of bacterial peritonitis (33%) and one case of catheter obstruction (10%). Barnett et al.(10) reported 29 patients, two catheters were inadvertently dislodged and there were two cases of abdominal wall cellulitis and one case of persistent leakage around the catheter. Joan L. Walker a, et al.(11) reported in large retrospective study including 205 patient where the peritoneal port-A-cath related complications that sometimes resulted in discontinuing peritoneal chemotherapy was seen in 40 patients (34 %) including catheter infection (n = 21), blocked catheter (n = 10); leaking catheter (n = 3); IP infusion leaking from vagina (n = 1); and port access problems (n = 5).

In our study Clinical success as regarding the response to chemotherapy was defined as improvement in tumor marker after receiving combined IV / IP chemotherapy, reduction in the grade/size of ascites and nodules if present before therapy. The later two judging points are well demonstrated on follow up by pelviabdominal CT.

In our study the complications related to chemotherapy was reported in 22.7 % of the cases. The most common peritoneal chemotherapy related complication that the patient experienced in our study was GIT upset and abdominal pain which occurred in three patients (13.6 %) and the second faced complication was serious neutropenia which occurred in two patients (9.09 %). Joyce N. Barlin et al.(12) reported in a large study including 102 patients receiving combined IV/IP showed neutropenia in 12 patients (12%); gastrointestinal related complications in 8 patients (8%) and neurological complications in 6 patient (6%). Deborah K. Armstrong et al.(13) reported discontinuation of peritoneal chemotherapy where 39 of

patients suffered from variable complications as GIT upset (abdominal pain , nausea , vomiting and dehydration) which was discovered in 20 patient ,metabolic and renal abnormalities which was discovered in 15 patient and bowel perforation which was experienced in 4 patients.

Our study tried to find out any statistical relevance between the incidence of peritoneal port related complications or chemotherapy related complications and its occurrence among two different age groups or regarding the tumor nature whether it is primary or recurrent and it was found out to be statistically insignificant as the P value among all the formentioned factors was  $> 0.05$  .

However , We found statistical significance as regarding the tumor marker level after peritoneal chemotherapy administration ( p value of tumor marker after peritoneal chemotherapy administration = 0.04 ) and we also concluded highly statistical significance as regarding the change in tumor marker level before and after peritoneal chemotherapy administration in relation to peritoneal chemotherapy related complication ( p value regarding tumor marker dC = 0.005), however there was no statistical significance as regarding the tumor marker level before peritoneal chemotherapy administration( p value of tumor marker before peritoneal chemotherapy administration = 0.724 ). Our study had a number of limitations. The data are somewhat biased because of the limited number of cases compared to other published

series due to the exclusion of a large number of patients who were not fit because of late presentation, presence of adhesions and the time factor .

Further more two patients were lost in the follow up and two cases died and the cause of death could not be clarified as they were not admitted to the hospital at time of death.

Financial issues hindered us from trying to focus with worrisome amount of peritoneal adhesions so as to save the peritoneal port-A-cath for patients that are considered more suitable candidates for peritoneal chemotherapy.

IBM SPSS statistics (V. 21.0, IBM Corp., USA, 2012) was used for data analysis. Data were expressed as Mean $\pm$ SD for quantitative parametric measures in addition to Median Percentiles for quantitative non-parametric measures and both number and percentage for categorized data.

The following tests were done:

1. Comparison between 2 dependent groups for parametric data using Paired t test.
2. Comparison between two independent groups for non-parametric data using Wilcoxon Rank Sum test.
3. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error at 0.05 was considered sig., while at 0.01 and 0.001 are highly significant.

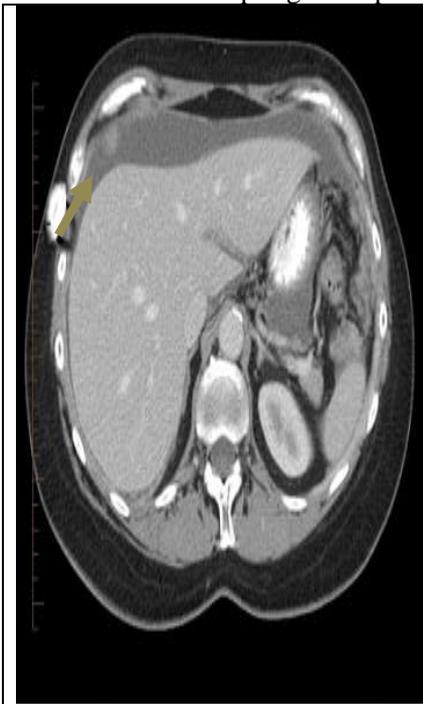
**Illustrative Cases**

**Case (1)**

A 54 years old female patient, known to have ovarian CA, underwent total abdominal hysterectomy with bilateral salpingoophorectomy 5 year's age, presented now with increased abdominal girth and loss of weight and appetite.

Pelviabdominal CT with contrast was done showing moderate free ascites and peritoneal nodules .Tumor marker (CA 125) was markedly elevated.

The patient was scheduled for peritoneal chemotherapy & was sent to the interventional radiology clinic for fluoroscopic guided peritoneal port-A-cath insertion.

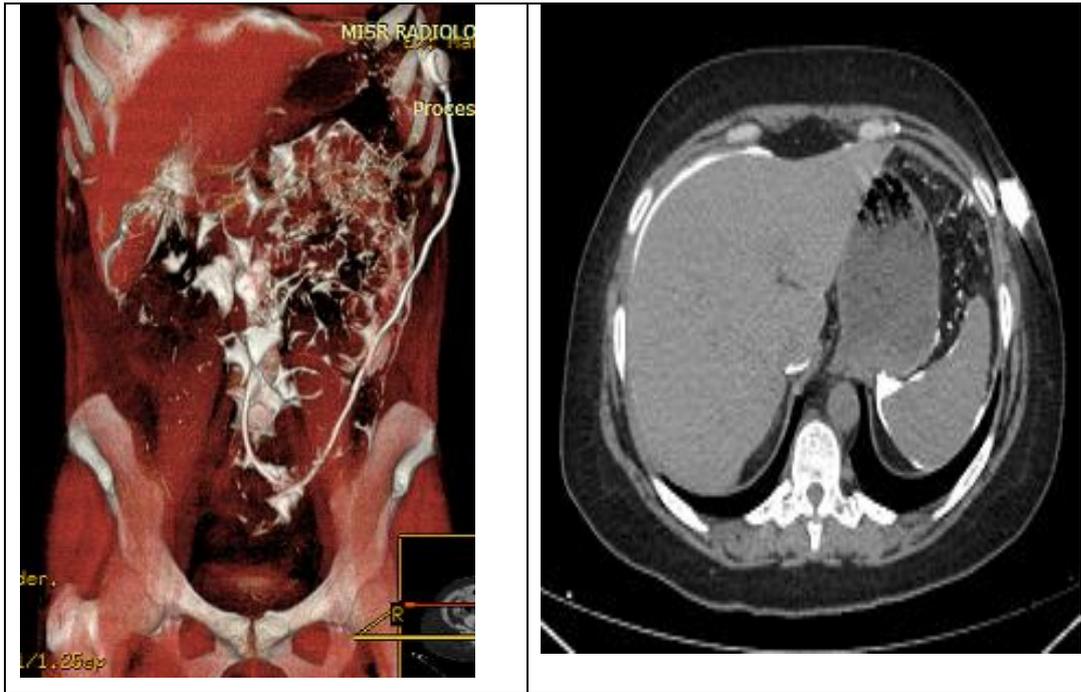
		
<p>Showing axial CT cuts with peritoneal deposit implicating the peritoneal reflection at the subphrenic region . Peritoneal port-A-cath is seen implanted over the right costal margin</p>	<p>Colored plate demonstrating reformed CT images with MIP reconstruction showing normal position of the implanted peritoneal port-A-cath over the right costal margin</p>	<p>showing axial CT cuts with total disappearance of peritoneal deposit that was seen implicating the peritoneal reflection at the subphrenic region</p>

**Case (2)**

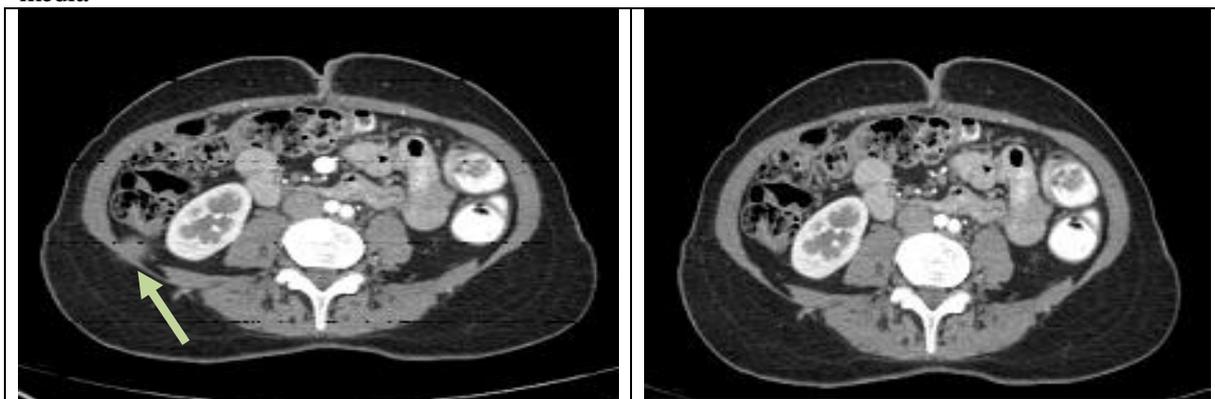
A 54 years old female patient , known to have ovarian CA , underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy 2 years ago and received post-operative IV chemotherapy, presented now with elevated CA 125.

Pelvi-abdominal CT with contrast was done showing solitary peritoneal nodule adherent to the inner aspect of the right lumbar region in great proximity to the right kidney.

The patient was scheduled for peritoneal chemotherapy & was sent to the interventional radiology clinic for fluoroscopic guided peritoneal port-A-cath insertion.



showing colored plate and conventional CT cuts showing good placement of the peritoneal port-A- cath and smearing of the peritoneal reflections after injection of diluted water soluble contrast media



showing arrowed peritoneal nodule < 1 cm related to the inner aspect of the right lumbar region in great proximity to the right kidney.

showing same axial CT cuts with total disappearance of the previously noted peritoneal nodule after 6 cycles of combined IV/IP chemotherapy.

## CONCLUSION

Ovarian cancer is one the most leading causes of death in females who develop gynecologic malignancies . This high mortality rate can be partially attributed to the fact that 75% of patients are diagnosed at an advanced stage of disease (i.e, Stage III or IV) , furthermore, despite a 80% remission rate with the recommended therapeutic approach, recurrence rates are high .

Significant improvement in disease control when chemotherapy is administered through the intraperitoneal route , making maximal surgical cytoreduction followed by systemic intravenous (IV) chemotherapy with a platinum agent and (IP) paclitaxel standard therapeutic approach.

Port catheters proved to be the most safe method of long term access to the peritoneal cavity with the lowest complication rate compared to other methods of access to the peritoneal cavity.

High technical success rate could be easily achieved by proper patient selection with efficient placement of the peritoneal port under fluoroscopic guidance with no need for general anesthesia.

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