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Research Article
Comparison of Key Sites Tumor Expansion on Imaging with Surgical Findings in Advanced Stage Ovarian Malignancy

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Abstract

Background and Objective: A number of key sites can be defined that are particularly involved and determined outcome of surgery. Pre-operative evaluation by advanced imaging (computed tomography/CT-scan or magnetic resonance imaging/MRI) is essential to plan. The objective of the study was to correlate the pre-operative CT-scan or MRI results to intraoperative findings. **Materials and Methods:** This was an observational study to correlate key sites of advanced ovarian epithelial cancer with intra operative. After ethical approval, imaging and operative data were obtained from medical record. **Results:** Sixty patients with advanced ovarian cancer were included in the study. Patients had CT-scan (75.0%) and MRI (25.0%). All patients were FIGO stage III and above during the operation. Analysis showed there were four key features that associated with the images significantly, mass at porta hepatis/gall bladder, massive ascites, lesion on subcapsular or intraparenchymal liver and large omental cake. Accuracy for the significant features was range between 65-81%. The specificity of the advanced imaging results was good all across the key sites but the sensitivity was considerably low. In the contrary, the sensitivity of images involving gastrointestinal tract was better than the sensitivity of lymph nodes involvement. **Conclusion:** Advanced imaging was specific in detecting epithelial ovarian malignancy spread pre-operatively although they were considerably low in sensitivity. Except, this study reported the high sensitivity and low specificity from the images of GI tract involvement. However, scrutinizing the advanced imaging findings systematically will benefit for surgical approach in particular for interdepartmental surgeon team.

Key words: Advanced ovarian cancer, CT-scan, MRI, primary debulking surgery, secondary debulking surgery, cytoreductive surgery

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The cornerstone treatment of advanced ovarian cancer is surgery up to no macroscopic residual disease at debulking surgery in combination with chemotherapy. The completeness of gross tumor evacuation acts as a free predictor of the survival rate. Therefore, maximal effort should be plan and done accordingly[1-4]. For better planning, an accurate evaluation of the extent of the disease is necessary. Studies have been shown that advanced imaging (CT-scan or MRI) is widely used as imaging modality for evaluation pre-operatively of advanced ovarian cancer[5-11]. In order to do proper debulking, a surgeon should have consideration of resectability, whether the disease can be resected optimally (no macroscopic disease). As proposed before, there are several methods proposed to predict the resectability of debulking surgery of advanced ovarian cancers, identification of key site implants, assessment of tumor load, combination of clinical features and advanced imaging features and identification of molecular signature associated with residual tumor[12]. The first until third method can be performed using imaging modality or direct visualization with laparoscopy. Advanced imaging modalities ultrasound, CT-including scan, MRI, PET-scan (Positron Emission Tomography) can be utilized for the purpose. Choice of imaging modalities depends on the hospital capacity beside the accuracy.

In current study it was investigated whether advanced imaging is corresponding to our findings during surgery. At to some extent, whether imaging can indeed capable of detecting 'key sites' which could be or not be resected during debulking surgery.

MATERIALS AND METHODS

This was an observational retrospective study on advanced stage ovarian cancer patients who had undergone primary debulking surgery from January, 2018 until June, 2019. Ethical clearance was released by Universitas Indonesia and Cipto Mangunkusumo Hospital, Jakarta, Indonesia. Subjects with incomplete data were excluded from the analysis. Some imaging criteria are crucial for advanced ovarian cancer in term of optimal debulking. Eleven criteria of peritoneal expansion were reviewed from soft copy results of advanced imaging (CT-scan or MRI), suprarenal or infrarenal paraaortic nodes lymph nodes >1 cm, diffuse small bowel adhesions/thickening, bowel mesentery lesion >1 cm, the root of the superior mesenteric artery lesion >1 cm, mass >1 cm on perisplenic area, lesser sac lesion >1 cm, mass $\geq$1 cm at porta hepatis or gall bladder, massive ascites, lesion on subcapsular liver of >1 cm or intraparenchymal liver lesion, lesion >1 cm on spleen and large omental cake (extended to spleen, gaster and lesser sac).

Statistical analysis: Analysis of these parameters was conducted against the presence of particular expansion during operation using Chi square analysis using SPSS Statistics 20. Accuracy between advanced imaging results and surgical findings were calculated using standard online statistical calculator program (© 2019 MedCalc Software bv).

RESULTS

Of the 113 subjects, 60 subjects were eligible and could be analyzed with complete data of imaging. Characteristics of the subjects were described in Table 1. Patient's median age was 54 (SD±10.44) years old. Most patients had FIGO stage IIIC disease (78.3%) and serous ovarian carcinoma (73.0%). Patients were managed with primary debulking (57, 95.0%) and the result was mostly optimal debulking (31, 51.7%).

Analysis of advanced imaging resulted in towards the presence of the key site for unresectable ovarian cancer was shown on Table 2. Univariate analysis found four significant key sites, mass $\geq$1 cm at porta hepatis or gall bladder, massive ascites, lesion on subcapsular liver of >1 cm or intraparenchymal liver lesion and large omental cake.

Table 1: Characteristics of the subjects total n = 60

Characteristics	Median (±SD)/N (%)
Age (years)	54.0±10.4
Ca125 (U mL^{-1})	534.5±1287.8
ASA status	
1	3 (5.26%)
2	29 (50.88%)
3	26 (45.61%)
Pathologic results	
Serous adenocarcinoma	44 (73.0%)
Mucinous adenocarcinoma	10 (16.7%)
Clear cell	4 (6.7%)
Endometrioid adenocarcinoma	2 (3.3%)
FIGO stage	
3 A	11 (18.3%)
3 C	47 (78.3%)
4 A	1 (1.7%)
4 B	1 (1.7%)
Type of advanced imaging	
CT-scan	43 (75.0%)
MRI	14 (25.0%)
Time of debulking procedure	
Primary debulking	57 (95.0%)
Interval debulking	3 (5.0%)
Type of debulking procedure	
Optimal debulking	31 (51.7%)
Suboptimal debulking	29 (48.3%)

Table 2: Key sites of advanced ovarian cancer extension and Intra-operative findings

		Intra-operative findings			
Key sites of extended diseases	Results	(+)	(-)	OR (CI 95%)	p-value
Suprarenal or infrarenal	+	10 (62.5%)	6 (37.5%)	2.39 (0.72-7.93)	0.42
paraaortic nodes >1 cm	-	16(41.0%)	23 (59.0%)		
Diffuse adhesion/thickening of	+	38 (76.0%)	12 (24.0%)	2.53 (0.50-10.90)	0.20
Small bowel	-	4 (50.0%)	4 (50.0%)		
Mass >1 cm on mesentery	+	13 (40.6%)	19 (59.3%)	1.29 (0.44-3.78)	0.64
	-	8 (32.0%)	17 (68.0%)		
Mass >1 cm on root of the	+	4 (40.0%)	6 (60.0%)	4.22 (0.91-19.51)	0.53
superior mesenteric artery	-	5 (11.6%)	38 (88.4%)		
Mass >1 cm on perisplenic area	+	1 (12.5%	7 (87.5%)	1.02 (0.11-9.84)	0.98
	-	6 (12.2%)	43 (87.5%)		
Mass >1 cm on lesser sac	+	2 (28.6%)	5 (71.4%)	2.05 (0.34-12.48)	0.43
	-	8 (17.0%)	41 (83.7%)		
Mass $\geq$1 cm on porta	+	9 (45.0%)	11 (55.0%)	14.32 (2.68-76.46)	0.00
hepatis/gall bladder	-	2 (5.4%)	35 (94.6%)		
Massive ascites	+	24 (77.4%)	7 (22.6%)	20.57 (5.32-79.55)	0.00
	-	4 (14.3%)	24 (85.7%)		
Lesion >1 cm subcapsular liver or	+	7 (35.0%)	13 (65.0%)	8.42 (1.73-51.35)	0.03
intraparenchymal liver	-	2 (5.4%)	35 (94.6%)		
Lesion >1 cm on spleen	+	1 (14.3%)	6 (85.7%)	2.50 (0.22-28.06)	0.44
	-	3 (6.2%)	45 (93.8%)		
Large omental cake	+	14 (46.7%)	16 (53.3%)	5.47 (1.53-19.59)	0.04
	-	4 (13.8%)	23 (86.2%)		

+: Present, -: Absent

Table 3: Sensitivity and specificity of the key sites advanced imaging results

Key sites	Sens	Spe	PPV	NPV	LR (+)	LR (-)	Accuracy
Suprarenal or infrarenal paraaortic nodes >1 cm	0.38	0.79	0.63	0.59	1.86	0.78	0.60
Diffuse adhesion/thickening of small bowel	0.90	0.25	0.76	0.50	1.21	0.38	0.72
Mass >1 cm on mesentery	0.62	0.47	0.41	0.68	1.17	0.81	0.53
Mass >1 cm on root of the superior mesenteric artery	0.44	0.86	0.40	0.88	3.26	0.64	0.79
Mass >1 cm on perisplenic area	0.14	0.86	0.13	0.88	1.02	1.00	0.77
Mass >1 cm on lesser sac	0.20	0.89	0.29	0.84	1.84	0.90	0.77
Mass $\geq$1 cm on porta	0.82	0.76	0.45	0.95	3.42	0.24	0.77
Hepatis/gall bladder							
Massive ascites	0.86	0.77	0.77	0.86	3.80	0.18	0.81
Lesion >1 cm subcapsular liver or intraparenchymal liver mass	0.78	0.73	0.35	0.95	2.87	0.30	0.74
Lesion >1 cm on spleen	0.25	0.88	0.14	0.94	2.13	0.85	0.84
Large omental cake	0.78	0.59	0.47	0.85	1.90	0.38	0.65

Sens: Sensitivity, Spec: Specificity, PPV: Positive predictive value, NPV: Negative predictive value, LR: Likelihood ratio

Table 3 showed the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. Accuracy for each of the significant predictors mentioned were 77% for mass $\geq$1 cm at porta hepatis or gall bladder, 81% for massive ascites, 74% for lesion on subcapsular liver of >1 cm or intraparenchymal liver lesion and 65% for large omental cake. The sensitivity of key sites involving gastrointestinal tract (small bowel adhesion/ thickening, mesentery mass and omental cake) was better than the sensitivity of lymph nodes involvement (paraaortic nodes and nodes near superior mesenteric artery). Although the specificity of all the parameters was quite high, the ones involving intestines were three of the bottoms (small bowel adhesion/thickening 0.25, mesentery mass 0.47, omental cake 0.59).

DISCUSSION

There were four significant key sites involvement in our study, mass $\geq$1 cm at porta hepatis or gall bladder, massive ascites, lesion on subcapsular liver of >1 cm or intraparenchymal liver lesion and large omental cake. All of these key sites were gastrointestinal involvement.

On the other hand, nodal involvement showed low number in both sensitivity and specificity of the pre-surgery imaging. The best accuracy and combination of sensitivity and specificity was showed by ascites (sensitivity 86%, specificity 77% and accuracy 81%). It was inevitable due to advanced state of the disease and the type of histopathology, serous adenocarcinoma majorly present in our study. This study showed that pre-operative study advanced imaging (CT-scan

or MRI) had high specificity despite the low sensitivity in depicting advanced ovarian cancer dissemination. Therefore, it suggested that if the pre-operative imaging results do not indicate disease, the absence of the disease on the key sites can be confidently assumed.

Previous study also suggested the similar data, pre-operative CT-scan showed high specificity but low sensitivity in detecting tumor dissemination[9,13-17]. Although, some key sites were significantly detected, mass $\geq$1 cm at porta hepatis or gall bladder, massive ascites, lesion on subcapsular liver of >1 cm or intraparenchymal liver lesion and large omental cake. Since almost the key sites of expansion involving gastrointestinal tract, involvement of good GI surgeon should be settled before operation. Currently, there was one study proposed to routine interpretation of staging CT-scan in preparation of advanced ovarian cancer[10]. It provides a systematic approach to identify tumor at key sites that predict that debulking will not be complete. That study suggested structured presentation to report the disease, sites of resectable disease in the pelvis, abdomen, retroperitoneum and chest if included, sites of on resettable disease in the same area, disease complications such as hydronephrosis, bowel obstruction etc., radiological FIGO stage and other significant findings.

Nevertheless, the aim of debulking surgery is no macroscopic disease (R0) or at least optimal debulking (R<1 cm) at the end of the operation. Preoperative resectability becomes really important in determining whether the approach will be primary or secondary debulking on advanced ovarian cancer surgery. Studies with large different kinds of criteria or parameters have been done to predict resectability of primary debulking surgery[5,16,18-20]. There were several methods proposed to predict resectability pre-operatively. One of them is identification of irresectable key site implants, using advanced imaging (ultrasound, CT-scan, MRI, PET-scan) or laparoscopy[12]. The sensitivity of key sites should reflect the ability to be resectable during operation.

CONCLUSION

High specificity values were shown in almost all parameter of advanced imaging findings despite the low sensitivity. However, the images involving GI tract were on the contrary. Images of small bowel adhesion/thickening, mesentery mass >1 cm and vast omental cake indicated high sensitivity but low specificity. Finally, advanced imaging can detect tumor reliably at various key sites that are predictive for resectability.

SIGNIFICANCE STATEMENT

This study presents comparison of pre-surgery advanced imaging and surgical findings. Gastrointestinal involvement key sites were significantly specific compared to the nodal involvement.

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