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Diaphragm disease in advanced ovarian cancer: Predictability of pre-operative imaging and safety of surgical intervention☆

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ABSTRACT

Objectives: To establish the positive predictive values of pre-operative identification with CT imaging of metastatic diaphragm disease in surgically managed cases of advanced ovarian cancer (AOC). Additionally, we have assessed the post-operative morbidity and survival following diaphragmatic surgical intervention in a large regional cancer centre in the United Kingdom.
Study design: A retrospective review of all cases of AOC with metastatic diaphragm disease surgically treated at the Pan-Birmingham Gynaecological Cancer Centre, UK between 1st August 2007 and 29th February 2016.
Results: A total of 536 women underwent surgery for primary AOC. Diaphragm disease was evident intra-operatively in 215/536 (40.1%) and 85/536 women (15.9%) underwent a procedure involving their diaphragm. Of these 85 cases, 38 peritoneal strippings (38/85, 44.7%), 31 partial diaphragmatic resections (31/85, 35.6%) and 16 electro-surgical ablations (16/85, 18.9%) were performed. There were no significant differences in post-operative complications between the three different diaphragmatic surgical groups. Of those patients who underwent peritoneal stripping or partial diaphragm resection, 12% were upstaged to stage 4A by virtue of pleural invasion.
The positive predictive value for pre-operative radiological identification of diaphragmatic disease was 78.6%. CT imaging failed to detect diaphragmatic involvement despite obvious diaphragm disease during surgery in 29.4% of cases, giving a low negative predictive value of 64.8%. The sensitivity and specificity for CT imaging in detecting diaphragm disease was 44.3% and 93.8%, respectively.
Conclusions: Diaphragmatic disease is often discovered in AOC. However, pre-operative assessment with CT imaging is not reliable in accurately detecting diaphragm involvement. Therefore, all patients with AOC should be regarded as in potential need for diaphragm surgery and their operation undertaken in cancer centres with adequate expertise in upper abdominal surgery. If there is a suspicion of diaphragm muscle invasion during diaphragmatic peritonectomy, the muscle should be partially resected. This will lead to potential upstaging of disease to stage 4A and therefore, to suitability for targeted therapy. In our Centre, the surgical removal of diaphragmatic disease did not significantly increase surgical morbidity.

Introduction

Survival in advanced ovarian cancer (stage 3B, 3C and 4 ovarian, tubal and peritoneal cancer – AOC) is dependent on residual disease following cytoreductive surgery [1–3]. Eliminating all macroscopic disease in the peritoneal cavity leads to improved prognosis in AOC and therefore, complete cytoreduction (zero macroscopic residual disease) is the key surgical aim of AOC treatment [4–8]. Cytoreduction rates in AOC have increased following the addition of upper abdominal surgical procedures, thereby improving survival in patients who would otherwise be rendered suboptimally cytoreduced [2,6,9].

Upper abdominal metastatic disease typically occurs via transcoelomic spread, through the transfer of malignant cells in peritoneal fluid and by direct extension of disease along peritoneal surfaces [6,10]. There is a high incidence of diaphragm involvement

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Table 1
Population characteristics, pathology results and surgical outcomes.

	Diaphragmatic resection N = 31 (36.5%)	Peritoneal stripping N = 38 (44.7%)	Ablation N = 16 (18.9%)	P Value	Rest of patients N = 451
Age (years) (Mean ± SD)	58.6 ± 10.1	60.3 ± 9.5	62.0 ± 12.8	0.3679	63.5 ± 2.38
ASA (Median ± IQR)	2 (1.5–2)	2 (2–3)	2 (2–2.5)	0.3230	2 (2–3)
BMI (Median ± IQR)	25.5 (23–28.5)	25.5 (21–28.5)	26 (22–29)	0.3679	26 (22–29)
Stage	**n (%)**	**n (%)**	**n (%)**	0.0305	**n (%)**
3B	1 (3.2)	2 (5.3)	4 (25.0)		56 (12.4)
3C	15 (48.4)	29 (76.3)	8 (50.0)		289 (64.1)
4	15 (48.4)	7 (18.4)	4 (25.0)		106 (23.5)
Organ of Origin	**n (%)**	**n (%)**	**n (%)**	0.8312	**n (%)**
Ovary	16 (51.6)	27 (71.1)	11 (68.8)		318 (70.5)
Peritoneum	3 (9.7)	4 (10.5)	2 (12.5)		78 (17.3)
Fallopian Tube	12 (38.7)	7 (18.4)	3 (18.8)		55 (12.2)
Grade	**n (%)**	**n (%)**	**n (%)**	0.4473	**n (%)**
Low (G1)	2 (6.5)	4 (10.5)	0 (0.0)		17 (3.8)
High (G2-3)	29 (93.5)	34 (89.5)	16 (100.0)		434 (96.2)
Histological Sub-type	**n (%)**	**n (%)**	**n (%)**	0.2642	**n (%)**
Serous	28 (90.3)	35 (92.1)	15 (93.8)		391 (86.7)
Clear cell	0 (0.0)	0 (0.0)	1 (6.3)		20 (4.4)
MMT	3 (9.7)	2 (5.3)	0 (0.0)		28 (6.2)
Undifferentiated	0 (0.0)	1 (2.6)	0 (0.0)		12 (2.7)
Surgery Type	**n (%)**	**n (%)**	**n (%)**	0.3768	**n (%)**
Primary	12 (38.7)	12 (31.6)	8 (50.0)		153 (33.9)
IDS	19 (61.3)	26 (68.4)	8 (50.0)		298 (66.1)
Cytoreduction	**n (%)**	**n (%)**	**n (%)**	0.5543	**n (%)**
R0	30 (96.8)	34 (89.5)	13 (81.3)		275 (61.0)
R1	1 (3.2)	3 (7.9)	2 (12.5)		67 (14.9)
R2	0 (0.0)	1 (2.6)	1 (6.3)		109 (24.2)
Surgical Complexity[a]	**n (%)**	**n (%)**	**n (%)**	0.0172	**n (%)**
Low	2 (6.5)	2 (5.3)	5 (31.3)		352 (78.0)
Intermediate	10 (32.3)	19 (50.0)	6 (37.5)		83 (18.4)
High	19 (61.3)	17 (44.7)	5 (31.3)		16 (3.5)

[a] Surgical complexity as per Aletti's surgical complexity score [20].

in AOC [7]. In the EORTC 55971 study, diaphragmatic disease was seen in 71.0% and 42.3% of women with AOC during primary and interval debulking surgery, respectively [11].

Despite the frequency of diaphragmatic disease, it remains one of the common barriers to both optimal and complete cytoreduction [4,5,7,12]. Although the surgical resection of metastatic disease has been demonstrated to significantly increase 5-year survival in AOC [13], only 30% of gynaecological oncologists in the United Kingdom would treat diaphragm involvement upon detection [14]. Diaphragmatic surgery has a crucial role in cytoreduction and has acceptable and manageable complication and morbidity rates reported in the literature [10,15,16].

Questions remain as to the accuracy of pre-operative identification with CT imaging of metastatic diaphragm disease. The purpose of this study was to determine the positive predictive value (PPV) of preoperative imaging as well as the proportion of CT scans with false negative results in cases who underwent cytoreductive surgery. Additionally, we have assessed the post-operative morbidity and survival following treatment in a large regional cancer centre in the United Kingdom.

Materials and methods

A retrospective review was performed of all women with diaphragm metastasis who underwent surgery for AOC at the Pan-Birmingham Gynaecological Cancer Centre (PBGCC) between August 2007 and February 2016. Cases were identified from the centre's prospective database. Women were categorised as per the type of diaphragm surgery performed: (1) total peritonectomy with partial diaphragmatic resection, (2) total peritonectomy, (3) electrosurgical ablation/minor peritoneal resection. Patients who underwent surgery, either received (1) primary surgery followed by six cycles of adjuvant chemotherapy or (2) imaging-guided biopsy followed by three or four cycles

Table 2
Identification of diaphragm disease with pre-operative imaging.

Disease identification	Evidence intra-operatively	No evidence intra-operatively	Predictive Value
Suspicion on pre-operative imaging	66/507 (13.0%)	18/507 (3.6%)	PPV: 78.6% (66/84)
No suspicion on pre-operative imaging	149/507 (29.4%)	274/507 (54.0%)	NPV: 64.8% (274/423)