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Diagnosis and categorization of malignant effusions: A 6-year review from a single academic institution

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Abstract

Background: Cytologic detection of malignant cells in pleural, peritoneal, or pericardial effusion most likely indicates advanced stage of malignant disease. There are a few studies updating the categorization of malignant effusions.

Methods: The electronic pathology database was searched to identify consecutive cases of malignant effusion during a 6-year period. Patient age and gender, origins of known malignancy, and cytologic diagnoses were recorded and summarized.

Results: A total of 1059 specimens included 561 (53%) pleural, 441 (41.6%) peritoneal, and 57 (5.4%) pericardial fluids. Most of the pleural (516, 92.0%), peritoneal (418, 94.8%), and pericardial (53, 93.0%) specimens were derived from patients with a single known malignancy. More common origins involving pleural fluid were lung (152, 27.1%) followed by breast (103, 18.4%) and gastrointestinal tract (76, 13.5%). The most common etiology for women and men was breast (102, 30.8%) and lung (67, 36.2%), respectively. More common origins involving peritoneal fluid were gastrointestinal (158, 35.8%) and gynecologic (156, 35.4%) tracts, and breast (46, 10.4%). The most common etiology for women and men was Mullerian (156, 55.5%) and gastrointestinal tract (94, 68.6%), respectively. Most common origins involving the pericardial fluid were breast (20, 37.7%) and lung (17, 29.8%). Breast and lung were the most common etiology for women (20, 57.1%) and men (8, 44.4%), respectively.

Conclusions: Breast and lung remain to be the most common origin of both malignant pleural and pericardial effusion for women and men, respectively. The most common origin involving peritoneal effusion is Mullerian for women and gastrointestinal tract for men.

KEYWORDS

cytology of effusions, malignant effusions, pericardial fluids, peritoneal fluids, pleural fluids

1 | INTRODUCTION

Malignant cells in serous cavity fluids may be seen in patients with previously diagnosed malignancy or occur as the first presentation in patients with unknown malignancy. Cytologic examination of pleural, peritoneal, and pericardial fluids is the simplest tool for diagnosing malignant effusions. Detection of malignant cells in pleural, peritoneal, or pericardial fluids most likely indicates advanced stage of malignant disease and thus, significantly affects subsequent management plans. Based on 2018 National Cancer Institute cancer statistics, the five most common cancers are breast cancer, lung/bronchial tree cancer, prostate cancer, and colorectal cancer. However, there are a few studies updating the categorization of malignant effusions.[1] We reviewed all malignant pleural, peritoneal and pericardial cytology specimens examined in our laboratory from adult patients (>21 years old) during a 6-year period,

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aiming to report our institutional experience in cytological diagnosis and categorization of malignant effusions.

2 | MATERIALS AND METHODS

This study was approved by the Institutional Review Board at University of Michigan. The electronic pathology database was searched to identify consecutive cases of malignancy diagnosed in pleural, pericardial, and peritoneal effusion specimens at the University of Michigan between 1 June 2013 and 31 May 2019.

Each of the specimens consisted of one Diff-Quik-stained smear preparation, one ThinPrep slide preparation, and one H&E-stained cell block. The signing out pathologist determined whether immunocytochemical study would be performed for diagnosis and/or further categorization of malignancy. Each case was originally reviewed by the signing out pathologist and at least one additional pathologist who concurred with the diagnosis.

Patient demographics including patient age and gender were recorded for each case identified.

Electronic medical records were also reviewed to assist in determining and/or confirming the primary etiology of malignant cells for each case evaluated in this study. Pathology records were examined to identify whether a primary site of malignancy was indicated in each malignant effusion as well as whether immunohistochemistry was performed on the specimen. The frequencies of sites involving effusion specimens by specified and unspecified sites were calculated in correlation with patient history of malignancy.

3 | RESULTS

From the electronic medical record, 1200 cases of malignant pleural, peritoneal, and pericardial fluid were identified. The study cohort consisted of a total of 1059 cases after eliminating 141 cases from patients with repeat, multiple effusion specimens attributed to the same disease process. Of 1059 malignant effusions specimens, pleural fluid specimens represented the majority of the cohort (n = 561, 53%), followed by peritoneal fluid specimens (n = 441, 41.6%) and pericardial fluid specimens (57, 5.4%). The gender distribution among each subcohort is detailed in Table 1.

TABLE 1 Gender distributions of malignant effusions n (%)

Gender	Pleural effusions	Peritoneal effusions	Pericardial effusions
Female	359 (64.0)	298 (67.6)	36 (63.2)
Male	202 (36.0)	143 (32.4)	21 (36.8)
Total	561 (100)	441 (100)	57 (100)

3.1 | Pleural fluids

Most (516, 92.0%) of the malignant pleural effusion specimens were derived from patients with a single previously diagnosed malignancy (Table 2). Of these, 512 (99.2%) were attributed to the patient's known primary malignancy. Of the four cases attributed to a second malignancy, two patients with a history of breast cancer were found to have involvement by lung adenocarcinoma, one patient with extramedullary plasma cell myeloma was shown to have a carcinoma with a nonspecific immunoprofile, and one patient with a history of bladder cancer was found to have involvement by a lung adenocarcinoma. Of this cohort of patients with a single previously diagnosed malignancy, 331 (64.1%) were women and 185 (35.9%) were men. The most common primary site involving pleural fluid for the total cohort was lung (152, 29.5%), most of which were designated as adenocarcinomas (139, 91.4%). If sub stratified by gender, the most common etiology for a malignant pleural effusion for women was breast (102, 30.8% of women with a single previously diagnosed malignancy) and for men was lung (67, 36.2% of men with a single previously diagnosed malignancy). Of the 76 gastrointestinal primaries, pancreatic (29, 38.2%) and esophageal (23, 30.3%) etiologies were the most common. Of the 61 gynecologic primaries, the most common etiology was ovarian (36, 59%). Of the genitourinary primaries, the most common etiology was renal (15, 55.6%). Of the head and neck primaries, thyroid etiology was most common (10, 52.6% of head and neck primaries). Of these 10 cases, 5 were papillary thyroid carcinomas, 2 were anaplastic thyroid carcinomas, 1 was a medullary thyroid carcinoma, 1 was a follicular carcinoma, and 1 was an oncocytic carcinoma. The three salivary gland malignancies that involved the pleural fluid represented one case each of parotid adenocarcinoma, adenoid cystic carcinoma, and salivary duct carcinoma. While it is uncommon for sarcomas to involve effusion specimens, 9 (1.8%) cases of malignant effusions attributed to patients' known single primaries were due to sarcomas, 4 of which were undefined and the other 5 representing single cases defined as angiosarcoma, chondrosarcoma, desmoplastic small round blue cell tumor, epithelioid hemangioendothelioma, and Ewing's sarcoma.

Twenty-five (4.5%) of malignant pleural effusions were derived from patients with unknown primaries. Immunocytochemistry was performed in 16 (64%) cases. Only five cases resulted in specific designations after morphologic and/or immunohistochemical evaluation of the effusion specimen—two lung adenocarcinomas, two small cell carcinomas, and one adenocarcinoma of Mullerian origin. The remainder of these cases were not specifically classified to a primary site due to either lack of adequate cellularity on subsequent sections, nonspecific immunoprofiles, or lack of clinical impact in scenarios in which subtyping the malignancy would not impact clinical management (ie, patients with widespread malignant disease which would subsequently be managed by palliative care).

Twenty (3.5%) of malignant pleural effusions were derived from patients with multiple previously diagnosed primary malignancies. Table 3 lists distribution of cases with multiple primaries and respective cytologic results. 10 (50%) of these cases were attributed to lung, 2 (10%) to lymphoma, 1 (5%) to breast, and 1 (5%) to PTC. The remaining 6 (30%) cases had no specific designation with regards to

TABLE 2 Malignant pleural effusions in patients with a single previously diagnosed malignancy

Primary site	n (% of malignant pleural effusions)	M:F	Malignant effusion associated with primary (n)
Lung	152 (27.1)	67:85	152
Adenocarcinoma	139 (24.8)	60:29	139
Small cell carcinoma	7 (1.2)	5:2	7
Squamous cell carcinoma	3 (0.5)	1:2	2
Nonsmall cell carcinoma, unspecified	2 (0.4)	1:1	3
Sarcomatoid carcinoma	1 (0.2)	0:1	1
Breast	103 (18.4)	1:102	101
Gastrointestinal	76 (13.5)	40:36	76
Pancreatic adenocarcinoma	29 (5.2)	12:17	29
Esophageal adenocarcinoma	23 (4.1)	19:4	23
Gastric adenocarcinoma	10 (1.8)	5:5	10
Cholangiocarcinoma	5 (0.9)	0:5	5
Colorectal adenocarcinoma	3 (0.5)	2:1	3
Duodenal adenocarcinoma	2 (0.4)	0:2	2
Rectal adenocarcinoma	2 (0.4)	1:1	2
Gallbladder adenocarcinoma	1 (0.2)	0:1	1
Appendiceal adenocarcinoma	1 (0.2)	1:0	1
Gynecologic	61 (10.9)	0:61	61
Ovary	36 (6.4)	0:36	36
Uterine adenocarcinoma	7 (1.2)	0:7	7
Primary peritoneal carcinoma	6 (1.1)	0:6	6
Unspecified	4 (0.7)	0:4	4
Fallopian tube	3 (0.5)	0:3	3
Endometrial sarcoma	2 (0.4)	0:2	2
Carcinosarcoma	1 (0.2)	0:1	1
Vulvar adenocarcinoma	1 (0.2)	0:1	1
Bartholin gland adenocarcinoma	1 (0.2)	0:1	1
Hematologic	37 (6.6)	23:15	36
Diffuse large B-cell lymphoma	9 (1.6)	5:4	9
Plasma cell neoplasm	4 (0.7)	1:3	3
Mature B-cell lymphoma, unspecified	4 (0.7)	3:1	4
Acute lymphoblastic leukemia	3 (0.5)	2:1	3
Acute myeloid leukemia	2 (0.4)	2:0	2
Myeloid neoplasm	2 (0.4)	1:1	2
Plasmablastic lymphoma	2 (0.4)	2:0	2
Anaplastic large cell lymphoma	2 (0.4)	2:0	2
Mantle cell lymphoma	2 (0.4)	2:0	2
Leukemia, unspecified	1 (0.2)	1:0	1
Chronic myeloid leukemia	1 (0.2)	1:0	1
Chronic lymphocytic leukemia	1 (0.2)	0:1	1
Adult T-cell leukemia	1 (0.2)	0:1	1
Myeloid sarcoma	1 (0.2)	0:1	1
Mantle cell lymphoma	1 (0.2)	1:0	1
Follicular cell lymphoma	1 (0.2)	0:1	1
Genitourinary	27 (4.8)	19:8	26
Renal cell carcinoma	15 (2.7)	9:6	15
Urothelial cell carcinoma	6 (1.1)	4:2	5
Prostatic adenocarcinoma	6 (1.1)	6:0	6
Melanoma	25 (4.5)	13:12	25
Head and neck	19 (3.4)	13:6	19
Thyroid	10 (1.8)	4:6	10
Squamous cell carcinoma	6 (1.1)	6:0	6
Salivary gland	3 (0.5)	3:0	3
Mesenchymal lesion/sarcoma	9 (1.6)	5:4	9
Unspecified	4 (0.7)	1:3	4
Angiosarcoma	1 (0.2)	1:0	1
Chondrosarcoma	1 (0.2)	1:0	1
Desmoplastic small round blue cell tumor	1 (0.2)	1:0	1
Epithelioid hemangioendothelioma	1 (0.2)	1:0	1
Ewing's sarcoma	1 (0.2)	0:1	1
Neuroendocrine neoplasm	3 (0.5)	2:1	3
Mesothelioma	3 (0.5)	2:1	3
Thymic carcinoma	1 (0.2)	0:1	1

primary site on cytologic evaluation. Immunohistochemistry was performed in 13 (65%) of these cases, including 8 of the cases specified as lung primaries, 1 of the 2 cases specified as lymphoma, as well as the single cases specified as involved by breast and thyroid primaries.

3.2 | Peritoneal fluids

Similar to the cohort of malignant pleural fluid effusions, most (418, 94.8%) malignant peritoneal effusion specimens were derived from patients with a single previously diagnosed malignancy (Table 4). Of these, nearly all (415, 99.3%) were attributed to the patient's known primary malignancy. Of the three cases attributed to a second malignancy, one patient each with a history of breast cancer and colorectal carcinoma was diagnosed as having involvement by a Mullerian

TABLE 3 Malignant pleural effusions in patients with multiple previously diagnosed malignancies

Sites of malignancy	n (% of malignant pleural effusions)	M:F	Specified site involving fluid (n)
Lung + breast	4 (0.7)	0:4	Lung[2] Breast[1]
Lung + thyroid	3 (0.5)	0:3	Lung[1]
Lung + head and neck squamous cell carcinoma	2 (0.4)	2:0	Lung[2]
Lung + cervical squamous cell carcinoma	1 (0.2)	0:1	Lung
Lung + prostate	1 (0.2)	1:0	None
Breast + lymphoma	1 (0.2)	0:1	Lymphoma
Breast + papillary thyroid carcinoma	1 (0.2)	0:1	Papillary thyroid carcinoma
Prostate + salivary gland carcinoma	1 (0.2)	1:0	None
Prostate + lymphoma	1 (0.2)	1:0	Lymphoma
Lung + prostate + colorectal adenocarcinoma	1 (0.2)	1:0	Lung
Lung + prostate + esophageal adenocarcinoma	1 (0.2)	1:0	Lung
Lung + prostate + renal cell carcinoma	1 (0.2)	1:0	Lung
Lung + breast + renal cell carcinoma	1 (0.2)	0:1	Lung
Lung + colorectal adenocarcinoma + skin cancer	1 (0.2)	0:1	None

primary and the last case was a patient with a history of lymphoplasmacytic lymphoma who was diagnosed as having involvement by an adenocarcinoma of unknown etiology and nonspecific immunoprofile. Of this cohort of patients with a single previously diagnosed malignancy, 281 (67.2%) were women and 137 (32.8%) were men. The most common primary site involving the peritoneal fluid for the total cohort was the gastrointestinal tract (158, 35.8%), the most common specific organ of which was the pancreas (75, 47.5% of malignant peritoneal effusions attributed to gastrointestinal primaries). If substratified by gender, the most common etiology for a malignant peritoneal effusion for women was Mullerian (156, 55.5% of women with a single previously diagnosed malignancy) and for men was the gastrointestinal tract (94, 68.6% of men with a single previously diagnosed malignancy), the most common specific organ etiology being pancreatic (47, 34.3% of men with a single previously diagnosed malignancy). The least frequent primary malignancies involving the peritoneal fluid include one case of squamous cell carcinoma from the head and neck, one case of mesothelioma, and two cases of sarcoma (one being a synovial sarcoma, one being a leiomyosarcoma).

Fourteen (3.2%) of malignant peritoneal fluids were derived from patients with unknown primaries. Six (42.9%) underwent

TABLE 4 Malignant peritoneal fluids in patients with a single previously diagnosed malignancy

Primary site	n (% of malignant peritoneal fluids)	M:F	Malignant effusion associated with primary (n)
Gastrointestinal	158 (35.8)	94:64	157
Pancreatic adenocarcinoma	75 (17)	47:28	75
Gastric adenocarcinoma	25 (5.7)	16:9	25
Colorectal adenocarcinoma	17 (3.9)	8:9	16
Cholangiocarcinoma	14 (3.2)	8:6	14
Esophageal adenocarcinoma	11 (2.5)	10:1	11
Gallbladder adenocarcinoma	5 (1.1)	1:4	5
Rectal adenocarcinoma	3 (0.7)	1:2	3
Liver	3 (0.7)	2:1	3
Unspecified	3 (0.7)	1:2	3
Duodenal adenocarcinoma	2 (0.5)	0:2	2
Gynecologic	156 (35.4)	0:156	156
Ovary	101 (22.9)	0:101	101
Primary peritoneal carcinoma	22 (5)	0:22	22
Uterine adenocarcinoma	15 (3.4)	0:15	15
Fallopian tube	6 (1.4)	0:6	6
Unspecified	5 (1.1)	0:5	5
Carcinosarcoma	3 (0.7)	0:3	3
Cervix	2 (0.5)	0:2	2
Leiomyosarcoma	1 (0.2)	0:1	1
Vulva	1 (0.2)	0:1	1
Breast	46 (10.4)	0:46	45
Genitourinary	15 (3.4)	0:15	15
Urothelial cell carcinoma	7 (1.6)	0:7	7
Renal cell carcinoma	3 (0.7)	1:2	3
Prostatic adenocarcinoma	3 (0.7)	3:0	3
Testicular germ cell tumor	2 (0.5)	2:0	2
Hematologic	15 (3.4)	9:6	14
Diffuse large B-cell lymphoma	6 (1.4)	4:2	6
Acute myeloid leukemia	3 (0.7)	2:1	3
Anaplastic large cell lymphoma	3 (0.7)	2:1	3
Burkitt lymphoma	1 (0.2)	1:0	1
Plasma cell neoplasm	1 (0.2)	0:1	1
Lymphoplasmacytic lymphoma	1 (0.2)	0:1	0
Neuroendocrine neoplasm	11 (2.5)	7:4	11
Melanoma	7 (1.6)	6:1	7
Lung adenocarcinoma	6 (1.4)	6:0	6
Sarcoma	2 (0.5)	2:0	2
Leiomyosarcoma	1 (0.2)	1:0	1
Synovial sarcoma	1 (0.2)	1:0	1

TABLE 4 (Continued)

Primary site	n (% of malignant peritoneal fluids)	M:F	Malignant effusion associated with primary (n)
Head and neck squamous cell carcinoma	1 (0.2)	1:0	1
Mesothelioma	1 (0.2)	1:0	1

TABLE 5 Malignant peritoneal effusions in patients with multiple previously diagnosed malignancies

Sites of malignancy	n (% of malignant peritoneal effusions)	M:F	Specified site involving fluid
Breast + pancreas	2 (3.5)	0:2	Gastrointestinal tract/pancreas
Breast + primary peritoneal carcinoma	1 (1.8)	0:1	Mullerian
Breast + ovary	1 (1.8)	0:1	None
Breast + uterus	1 (1.8)	0:1	Mullerian
Lung + head and neck squamous cell carcinoma	1 (1.8)	0:1	Lung
Lung + primary peritoneal carcinoma	1 (1.8)	0:1	None
Uterus + cholangiocarcinoma	1 (1.8)	0:1	None
Breast + colon + primary peritoneal carcinoma	1 (1.8)	0:1	Mullerian

evaluation by ancillary testing, of which 4 (28.6%) resulted in specific designations for primary etiologies—1 primary effusion lymphoma, 2 gastrointestinal tract malignancies, and 1 Mullerian malignancy. The remainder of the cases was not specifically classified to a primary site either due to a lack of adequate cellularity on subsequent sections or nonspecific immunoprofiles.

Nine (2%) malignant peritoneal fluids were derived from patients with multiple previously diagnosed malignancies, the distribution of which are highlighted in Table 5. Of these, 6 (66.7%) were attributed to specific etiologies—3 (33.3%) Mullerian, 2 (22.2) gastrointestinal tract, and 1 lung adenocarcinoma (11.1%). The remaining three cases had no specific designation with regards to primary site on cytologic evaluation. Immunohistochemistry was performed in 8 (88.9%) of these cases, including all 6 cases with specified etiologies.

3.3 | Pericardial fluids

Similar to both the cohorts of malignant pleural and peritoneal fluids, the malignant pericardial fluid specimens were mostly (53, 93.0%) derived from patients with a single previously diagnosed malignancy (Table 6). Of these, nearly all (51, 96.2%) were attributed to the patient's known primary malignancy. Of the two cases attributed to a second malignancy, one patient with a lung cancer was shown to have involvement by an ovarian primary and one patient with a chronic lymphocytic leukemia was shown to have involvement by a lung adenocarcinoma. Of this cohort with a single previously diagnosed malignancy, 35 (66%) were women and 18 (34%) were men. The most common primary site involving the pericardial fluid for the total cohort was breast (20, 37.7%). If sub stratified by gender, the most common etiology for a malignant pericardial fluid was breast for women (20, 57.1% of women with a single previously diagnosed malignancy) and for men was lung (8, 44.4% of men with a single previously diagnosed malignancy). The least frequent primary malignancies involving the pericardial fluid were derived from a single case each of clear cell sarcoma, melanoma, and thymic carcinoma.

TABLE 6 Malignant pericardial effusions in patients with a single previously diagnosed malignancy

Primary site	n (% of malignant pericardial effusions)	M:F	Malignant effusion associated with primary (n)
Breast	20 (35.1)	0:20	20
Lung	17 (29.8)	8:9	16
Adenocarcinoma	14 (24.5)	6:8	14
Squamous cell carcinoma	1 (1.8)	1:0	1
Poorly differentiated nonsmall cell carcinoma	1 (1.8)	1:0	1
Sarcomatoid carcinoma	1 (1.8)	0:1	1
Hematologic	6 (10.5)	4:2	5
Diffuse large B-cell lymphoma	4 (7)	2:2	4
Chronic myelomonocytic leukemia	1 (1.8)	1:0	1
Chronic lymphocytic leukemia	1 (1.8)	1:0	1
Genitourinary	3 (5.3)	2:1	3
Urothelial cell carcinoma	2 (3.5)	1:1	2
Kidney	1 (1.8)	1:0	1
Gynecologic	2 (3.5)	0:2	2
Ovarian	1 (1.8)	0:1	1
Uterine	1 (1.8)	0:1	1
Gastrointestinal	2 (3.5)	2:0	2
Esophageal	2 (3.5)	2:0	2
Melanoma	1 (1.8)	1:0	1
Clear cell sarcoma	1 (1.8)	1:0	1
Thymic carcinoma	1 (1.8)	1:0	1

Three (7%) of malignant pericardial fluids were derived from patients with unknown primaries. One (33.3%) underwent evaluation by immunohistochemistry. None of the cases was specifically

classified to a primary site either due to a lack of adequate cellularity on subsequent sections or nonspecific immunoprofiles.

One (1.8%) of malignant pericardial fluids was derived from a patient with a history of prostate adenocarcinoma and squamous cell carcinoma of the head and neck. The immunohistochemical profile on this case was nonspecific, and therefore no specific designation for etiology was made on this specimen.

4 | DISCUSSIONS

A search of PubMed for publications focused on the distribution of malignant effusions published in the past two decades in the English language resulted in individual case reports, original studies consisting of relatively low number of malignant specimens, and limited reviews.[2-12] To investigate how the incidence of different types of malignancy involving malignant effusions has changed, Dermawan et al conducted a study consisting of malignant pleural, peritoneal and pericardial effusions diagnosed during a 17-year (2000-2016) period. The resultant 3285 malignant cases included 2175 (66.2%) pleural, 955 (29.1%) peritoneal and 155 (4.7%) pericardial fluids. Known primary sites were documented in 1023 (31%) cases, consisting of 648 (63.3%) pleural, 267 (26.1%) peritoneal and 108 (10.6%) pericardial fluids. The most common metastatic tumors in pleural fluid were lung for males and breast for females; in peritoneal fluid, hematolymphoid for males and Mullerian tumors for females; in pericardial fluid, lung for both genders.[1] In comparison with these findings, the present study consisted of a total of 1059 malignant effusion specimens originally diagnosed during a 6-year period (2013-2019), including 561 (53%) pleural, 441 (41.6%) peritoneal and 57 (5.4%) pericardial fluids. Of these, 986 (93.1%) effusions (516 pleural, 418 peritoneal, 53 pericardial) had a single previously diagnosed malignancy and 978 (92.4%) effusions (512 pleural, 415 peritoneal, 51 pericardial) were attributed to the patients' known primary malignancy. The latter findings reflected a greater frequency in primary sites identification of the malignant effusions. Review of morphological features along with the immunoprofiles and provided clinical history of malignancy played an important role in this regard. Similar to the aforementioned study, our data showed the most common etiology involving pleural effusions for women and men was breast and lung, respectively. Further, both studies showed the most common etiology involving peritoneal effusion was Mullerian for women. In contrast to the aforementioned study that showed hematolymphoid malignancy involving peritoneal fluids as the most common etiology of malignant peritoneal effusions for men, our study demonstrated gastrointestinal tract as the most common etiology for men. Last but not the least, the aforementioned study showed lung as the most common origin involving pericardial fluid in both women and men. The same findings were also reported by others.[6] However, our study revealed a similar trend in men (lung as the most common etiology) but not in women (breast as the most common etiology). Saab et al reported their findings in malignant pericardial effusion which were similar as ours.[11] Overall, the differences observed in these studies may be related to variations in patient populations included in the study cohorts. It is crucial for pathologists to have a clear understanding of practice patterns in their own institutions.

The malignant effusion specimens included in the current study were submitted with a wide range of volumes (1-2000 mL). In theory, any volume is considered optimal if a malignant diagnosis is rendered. To ensure an adequate cytology evaluation and minimize the possibility of false-negativity, a pleural fluid volume of ≥75 mL and a pericardial fluid volume of >60 mL is recommended by the authors from the same institution.[13,14] Utilization of different preparation methods for cytologic assessment of serous effusions has been reported. Dadhich et al compared their experience on conventional cytopreparatory and liquid based cytology. They did not find a significant difference in terms of cellularity, cell distribution or frequency of diagnosis of malignancy.[15] Lee et al claimed that the CellprepPlus method highlighted characteristic morphological features of malignant cells and provided high cellularity, which allowed for improved diagnostic accuracy in the evaluation of effusion cytology compared to the ThinPrep method.[16] Our effusion specimens were processed as one Diff-Quick-stained smear, one ThinPrep preparation and one H&E-stained cell block slide. The combination of different preparations appeared to provide an acceptable performance. However, it is beyond the scope of the current study to investigate diagnostic yield of various preparations.

The importance of immunocytochemistry combined with clinical history and cytomorphologic features in the work up of effusion specimens has been reviewed and discussed by Sundling and Cibas.[17] The same approach recommended by them was used when assessing the malignant effusion specimens contained in the current study. Immunocytochemistry was performed on the cell block preparation in an appropriate context, that is, to confirm the primary site in patients with a single known malignancy, evaluate for potential new primaries in patients with a known malignancy and a newly presenting mass lesion at another site, or to identify the origin in patients with multiple previously diagnosed malignancy or without known history of malignancy. Accordingly, application of immunocytochemistry in selected cases (29 of 45 pleural, 14 out of 23 peritoneal, and 2 out of 4 pericardial fluids) with sufficient cellularity on cell block material helped to specify the primary site in 9 out of a total of 23 malignant effusion specimens collected form the patients without previous history of malignancy; as well as in 14 out of a total of 23 malignant effusion specimens obtained from the patients with multiple known malignancies. In additional to immunocytochemistry, serous effusion cytology is considered to be suitable for molecular testing, and thus plays an important role in the era of personalized medicine.[18,19]

In conclusion, breast and lung remains to be the most common origin of both malignant pleural and pericardial effusion for women and men, respectively. The most common origin involving peritoneal effusion is Mullerian for women and gastrointestinal tract for men. Application of immunocytochemistry, along with review of cytomorphological findings and clinical history enhances the diagnostic accuracy of cytologic diagnosis.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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REFERENCES

1. Dermawan JKT, Policarpio-Nicolas ML. Malignancies in pleural, peritoneal, and pericardial effusions: a 17-year single-institution review from 30 085 specimens. *Arch Pathol Lab Med*. 2020.
2. Das DK. Serous effusions in malignant lymphomas: a review. *Diagn Cytopathol*. 2006;34(5):335-347.
3. Khalbuss WE, Yang H, Lian Q, Elhosseiny A, Pantanowitz L, Monaco SE. The cytomorphologic spectrum of small-cell carcinoma and large-cell neuroendocrine carcinoma in body cavity effusions: a study of 68 cases. *Cytojournal*. 2011;8:18.
4. Davion S, Rohan S, Nayar R, Kulesza P. Metastatic chromophobe renal cell carcinoma in pleural fluid cytology: review of literature and report of a case. *Diagn Cytopathol*. 2012;40(9):826-829.
5. Gupta S, Sodhani P, Jain S. Cytomorphological profile of neoplastic effusions: an audit of 10 years with emphasis on uncommonly encountered malignancies. *J Cancer Res Ther*. 2012;8(4):602-609.
6. Dragoescu EA, Liu L. Pericardial fluid cytology: an analysis of 128 specimens over a 6-year period. *Cancer Cytopathol*. 2013;121(5):242-251.
7. Lew M, Pang JC, Roh MH, Jing X. Cytologic features and immunocytochemical profiles of malignant effusions with metastatic papillary thyroid carcinoma: a case series from a single institution. *Acta Cytol*. 2015;59(5):412-417.
8. Policarpio-Nicolas ML, Avery DL, Hartley T. Merkel cell carcinoma presenting as malignant ascites: a case report and review of literature. *Cytojournal*. 2015;12:19.
9. Harbhajanka A, Brickman A, Park JW, Reddy VB, Bitterman P, Gattuso P. Cytomorphology, clinicopathologic, and cytogenetics correlation of myelomatous effusion of serous cavities: a retrospective review. *Diagn Cytopathol*. 2016;44(9):742-747.
10. Raymond SLT, Au K, Fu R, Tauchi-Nishi PS. Metastatic genitourinary cancer diagnosed by body fluid cytology: clinicopathologic and cytomorphologic correlation. *J Am Soc Cytopathol*. 2017;6(2):48-58.
11. Saab J, Hoda RS, Narula N, et al. Diagnostic yield of cytopathology in evaluating pericardial effusions: clinicopathologic analysis of 419 specimens. *Cancer Cytopathol*. 2017;125(2):128-137.
12. Li JJX, Chan WC, Chau HHL, Wu C, Tse GM. Cytologic diagnosis of metastatic malignant phyllodes tumor of the breast in pleural effusion. *Diagn Cytopathol*. 2019;47(6):599-602.
13. Rooper LM, Ali SZ, Olson MT. A minimum fluid volume of 75 mL is needed to ensure adequacy in a pleural effusion: a retrospective analysis of 2540 cases. *Cancer Cytopathol*. 2014;122(9):657-665.
14. Rooper LM, Ali SZ, Olson MT. A minimum volume of more than 60 mL is necessary for adequate cytologic diagnosis of malignant pericardial effusions. *Am J Clin Pathol*. 2016;145(1):101-106.
15. Dadhich H, Toi PC, Siddaraju N, Sevvanthi K. A comparative analysis of conventional cytopreparatory and liquid based cytological techniques (sure path) in evaluation of serous effusion fluids. *Diagn Cytopathol*. 2016;44(11):874-879.
16. Lee YM, Hwang JY, Son SM, et al. Comparison of diagnostic accuracy between CellprepPlus(R) and ThinPrep(R) liquid-based preparations in effusion cytology. *Diagn Cytopathol*. 2014;42(5):384-390.
17. Sundling KE, Cibas ES. Ancillary studies in pleural, pericardial, and peritoneal effusion cytology. *Cancer Cytopathol*. 2018;126(suppl 8):590-598.
18. Porcel JM. Diagnosis and characterization of malignant effusions through pleural fluid cytological examination. *Curr Opin Pulm Med*. 2019;25(4):362-368.
19. Siddiqui MT, Schmitt F, Churg A. Proceedings of the American Society of Cytopathology companion session at the 2019 United States and Canadian Academy of Pathology annual meeting, part 2: effusion cytology with focus on theranostics and diagnosis of malignant mesothelioma. *J Am Soc Cytopathol*. 2019;8(6):352-361.

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