Case series

Associated characteristics and impact on recurrence and survival of free-floating tumor fragments in the lumen of fallopian tubes in Type I and Type II endometrial cancer

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ABSTRACT

Objective: This study sought to evaluate characteristics of cases of free-floating tumor fragments within the lumen of fallopian tubes ('floaters') on final pathology for Type I and Type II endometrial adenocarcinoma, including relationships with disease recurrence and mortality.

Methods: A single institution experience of 1022 consecutive cases of uterine cancer presenting between 2005 and 2010 was retrospectively reviewed, with data extraction from electronic medical records. Associations of floaters with baseline characteristics were studied with logistic regression, and relationships with disease recurrence and survival were assessed with Cox proportional hazards models.

Results: Among 816 included cases of Type I or Type II endometrial adenocarcinoma, floaters were identified on final pathology for 20 patients (2.5%). Patient characteristics of cases with floaters mirrored the overall sample. With adjustment, presence of floaters trended towards association with laparoscopic/robotic approach (OR = 3.84; 95%CI 0.98-15.1), and was significantly associated with lymphovascular invasion (OR = 9.65; 95%CI 2.35-39.6) and higher stage disease. Although floaters were associated with increased risk of recurrence in unadjusted analysis (HR = 3.22; 95%CI 1.41-7.37), after adjustment for disease type, stage, and patient comorbidities, no evidence for impact on disease recurrence or overall survival was found.

Conclusions: The presence of floaters is rare. Floaters were generally associated with more extensive disease, but no evidence was found to show any independent prognostic impact on risk of recurrence or death. In agreement with prior research, this study found a trend towards association of floaters with laparoscopic/robotic approach, indicating the possibility of floaters sometimes being the result of trauma from uterine manipulator insertion.

1. Introduction

Endometrial cancer is the most common gynecologic malignancy among women in the United States and accounts for 6% of malignancies in women worldwide. In the United States in 2017, 61,380 women will be diagnosed with endometrial cancer and 10,920 women will succumb to the disease (Siegel et al., 2014).

Endometrial cancers exist in two forms, Type I and Type II (Bokhman, 1983). Type I disease (65–70% of all cases) includes International Federation of Gynecology and Obstetrics (FIGO) grade 1 and FIGO grade 2 endometrioid histology, and is often associated with

unopposed estrogen exposure (Lax et al., 1998; Voss et al., 2012; Goff et al., 1994). Type II disease includes FIGO grade 3 endometrioid, serous, or clear cell histology, and has a different genetic profile with development thought to be independent of estrogen exposure. Type II endometrial cancer is typically more aggressive than type I cancer and has a poorer prognosis (Mutch, 2012; Wilson TO et al., 1990; Emons et al., 2000; Hameed and Morgan, 1972; Hamilton et al., 2006).

In 2009, updated staging recommendations were released by FIGO that made a series of small changes to the system, including eliminating a role for positive cytology from peritoneal washings in upstaging disease to stage IIIA (Creasman, 2009; Pecorelli et al., 2009). Another

pathologic finding that is sometimes noted on pathology reports is the presence of free floating fragments of tumor within the lumen of one or both fallopian tubes (Zaino, 2009). A body of literature has accumulated assessing the role of positive cytology in prognosis, ultimately finding a relatively small impact in otherwise early stage disease, not warranting upstaging. On the other hand, research is lacking into the role of floaters in prognosis, as well as associations with other characteristics of the patient and case.

The true incidence and etiology of floaters is unknown. In the only study of its kind, in 2013, DeLair et al. explored the difference in the incidence of floaters in laparoscopic (LH) versus robotic-assisted (RH) surgery for endometrial cancer (Delair et al., 2013). They found the incidence of floaters in LH to be 2.2% versus 11.7% in RH (P < 0.001). The majority of the patients with RH and tumor present in the tubes had Stage I disease (9/16, 56.2%) and Grade 1 tumors (9/16, 56.2%). Patients with floaters had a non-statistically significant higher body mass index. The authors postulated that floaters were a contaminant secondary to the placement of a uterine manipulator and also uterine manipulation, which they postulated was higher in RH (Delair et al., 2013; Sonoda et al., 2001; Lim et al., 2008).

The objective of this study was to examine a series of cases with the finding of floaters on final pathology within a cohort of endometrial cancer patients in order to better understand the role of floaters in disease, including associations with patient, surgical, and pathologic characteristics, and assessment for impact on outcomes of time to progression and overall survival.

2. Methods

2.1. Study design

This study represents the experience of a single health system (Yale New Haven Health including Yale New Haven Hospital and the affiliated Bridgeport Hospital) with a new diagnosis of uterine cancer over a six year period. A retrospective cohort was formed from consecutive patients presenting to the health system's Division of Gynecologic Oncology with uterine cancer between January 1, 2005 and December 31, 2010. Diagnosis of pathologic subtype of uterine cancer was performed by trained gynecologic pathologists and all cases were reviewed at a multidisciplinary tumor board. This sample included both patients with preoperative biopsy showing uterine cancer followed by benign final pathology at the time of surgery, as well as patients with no sampling or benign preoperative pathology, and invasive cancer on final pathology of the surgical specimen. Study follow up was completed at the start of data extraction, defined as June 1st, 2016.

2.2. Data extraction

Institutional Review Board (IRB) approval was obtained before starting the study. Data was manually extracted from electronic health records. Extracted data included baseline patient characteristics, treatment, and outcomes (age, gravidity, parity, menopausal status, BMI, OCP use, HRT use, smoking status, medical and surgical history, adjuvant treatment, recurrence, death) from provider clinic and hospital notes, surgical characteristics (surgeon, approach, additional procedures) from operative notes, and pathological characteristics from preoperative, frozen, and final pathology notes. It should be noted that the presence of "floaters" on final pathology had no impact on the stage assigned to a patient as the International Federation of Gynecology and Obstetrics (FIGO) does not consider it in their staging system. The FIGO 2009 staging system was used for all patients (Creasman, 2009). Dates of death were confirmed with publically available obituary data. For patients lost to follow up, the date of last contact was used for the date of censure. For patients known to have died, but with no identifiable date of death, the date of last contact was approximated as the date of

Table 1
Demographic characteristics of single institution cohort of patients with type I and type II endometrial adenocarcinoma, by presence or absence of floaters.[a]

	Floaters	No floaters	P value
	(n = 20)	(n = 796)	
Age at diagnosis (years)	65.6 (12.9)	63.3 (11.5)	0.38
Race (%)			0.32
White	85.0%	84.0%	
Black	5.0%	8.7%	
Hispanic	10.0%	2.8%	
Asian	0%	1.4%	
Other	0%	3.2%	
Gravidity	1.85 (1.63)	2.29 (1.88)	0.30
Parity	1.70 (1.53)	1.89 (1.78)	0.60
Body mass index (kg/m^2)	34.2 (8.6)	33.6 (12.2)	0.85
Menopausal (%)	90.0%	85.5%	0.57
Smoker (≥ 5 pack-years, %)	35.0%	24.1%	0.26
HRT use (> 3 months, %)	18.8%	21.6%	0.79
OCP use (> 3 months, %)	26.7%	31.4%	0.70
Medical history (%)			
Hypertension	65.0%	58.8%	0.58
Diabetes	45.0%	23.8%	0.03
Major CV disease[b]	10.5%	5.2%	0.30
Psychiatric disease[c]	10.5%	8.7%	0.77
Other cancer	15.8%	10.1%	0.42
Prior abdominal surgery	35.0%	38.4%	0.76

HRT = hormone replacement therapy; OCP = oral contraceptive pills.
[a] For continuous variables, mean (standard deviation) shown, Student's *t*-test for significance; for dichotomous and categorical variables, percent with characteristic shown, Pearson's χ^2 test for significance. Floaters were defined as evidence of free-floating tumor fragments within the fallopian tubes on final pathologic specimen analysis.
[b] Includes history of congestive heart failure, myocardial infarction, and stroke.
[c] Includes diagnoses of depression, anxiety, bipolar, and schizophrenia.

death. Data extraction was performed in parallel by four researchers (BA, JB, SG, MW, RP) in a standardized fashion using a single data entry form.

2.3. Study sample

The analysis in this study was performed on a subset of the above described cohort of patients with endometrial cancer, limited to patients with Type I (FIGO Grade 1 and 2 endometrioid adenocarcinoma) or Type II (FIGO Grade 3 endometrioid adenocarcinoma, clear cell carcinoma of the endometrium, uterine papillary serous carcinoma, and mixed endometrial carcinomas) disease. Patients with uterine sarcomas, carcinosarcomas, and squamous cell carcinomas were excluded. The study sample was further limited by excluding patients with missing data for variables critical for defining the type of disease (cellular histology on the final pathologic specimen), and for determining the outcome in time-to-event analysis (date of diagnosis and current disease status).

2.4. Analyses

The primary characteristics of interest in this study was the presence or absence of 'floaters.' For the purposes of this study, 'floaters' was defined as the presence of free floating tumor fragments identified within the fallopian tubes on sectioning and final pathological analysis of the specimen. Baseline characteristics of patients having pathology with and without the presence of floaters were compared using Student's *t*-test for continuous variables, and Pearson's χ^2 test for dichotomous and categorical variables. Descriptive statistics were used to describe the prevalence of floaters by cancer stage and nuclear grade at the time of surgery, as well as the relationship to positive peritoneal cytology. Of note, peritoneal cytology status was not originally included in the extracted data and was only assessed and available for cases with the presence of floaters. Associations of the presence of floaters with

Table 2
Case distribution, by presence or absence of floaters,[a] for single institution cohort of patients with type I and type II endometrial adenocarcinoma, 2005–2010.

	Type I		Type II	
	(n = 550)		(n = 266)	
	No floaters	Floaters	No floaters	Floaters
	(n = 544; 98.9%)	(n = 6; 1.1%)	(n = 252; 94.7%)	(n = 14; 5.3%)
Stage				
I	421 (77.4%)	4 (66.7%)	139 (55.2%)	3 (21.4%)
II	55 (10.1%)	0	20 (7.9%)	1 (7.1%)
III	53 (9.7%)	2 (33.3%)	53 (21.0%)	5 (35.7%)
IV	11 (2.0%)	0	33 (13.1%)	5 (35.7%)
X/Unstaged	4 (0.8%)	0	7 (2.8%)	0
FIGO grade				
Grade 1	305 (56.1%)	1 (16.7%)	0	0
Grade 2	239 (43.9%)	5 (83.3%)	0	0
Grade 3	0	0	252 (100%)	14 (100%)
Nuclear grade				
Grade 1	82 (15.1%)	0	0	0
Grade 2	425 (76.3%)	5 (83.3%)	21 (8.3%)	0
Grade 3	44 (8.1%)	1 (16.7%)	227 (90.1%)	14 (100%)
Pelvic washings[b]				
Positive	–	1 (16.7%)	–	6 (42.9%)
Negative	–	5 (83.3%)	–	8 (57.1%)
Surgery type				
Abdominal/Vaginal	347 (63.8%)	2 (33.3%)	199 (80.0%)	9 (64.3%)
Laparoscopic/Robotic	190 (34.9%)	4 (66.7%)	49 (19.4%)	5 (35.7%)

[a] Floaters were defined as evidence of free-floating tumor fragments within the fallopian tubes on final pathologic specimen analysis.
[b] Pelvic washing status data only recorded for cases with presence of floaters.

surgical and pathologic characteristics were investigated using bivariate and multivariate logistic regression.

For primary analyses, time-to-event analysis was performed using the dates of diagnosis, progression, lost to follow up, and death. Bivariate and multivariate Cox proportional hazards models were created to assess the association of different patient and disease characteristics on the risk of progression and death. For all analyses, the date of diagnosis represented time zero and was defined as the date of tissue sampling showing endometrial cancer, whether disease was first identified on preoperative endometrial sampling or at the time of hysterectomy on frozen or final pathological analysis.

For time to progression analysis, yielding hazard ratios for risk of progression, failure was defined by disease recurrence or progression, and patients were censored at date of lost to follow up or death without disease recurrence or progression. In addition to our primary exposure of floaters on final pathology, other risk factors for progression were considered, including cancer type and stage, and patient age and race.

For overall survival analysis, yielding hazard ratios for risk of death, failure was defined by death from any cause, and patients were censored at date of lost to follow up. In addition to aforementioned risk

Table 3
Associations of presence of floaters[a] with surgical approach and pathological characteristics in a single institution cohort of patients with type I and type II endometrial adenocarcinoma, 2005–2010.[a]

	Bivariate		Multivariate	
	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Surgical approach				
Abdominal/Vaginal	ref.		ref.	
Laparoscopic/Robotic	1.87 (0.76–4.57)	0.17	3.84 (0.98–15.1)	0.05
Type				
Type I	ref.		ref.	
Type II	5.04 (1.91–13.3)	0.001	1.77 (0.21–14.6)	0.60
Nuclear grade				
Grade 1/2	ref.		ref.	
Grade 3	5.73 (2.06–15.9)	0.001	5.92 (0.53–66.4)	0.15
+ Lymphovascular Invasion	2.94 (1.20–7.17)	0.02	9.65 (2.35–39.6)	0.002
+ Lower Uterine Segment Invasion	1.16 (0.45–2.95)	0.76	0.89 (0.24–3.40)	0.87
Myometrial Invasion Depth (0–100%)[b]	0.33 (0.06–1.75)	0.19	0.08 (0.01–0.60)	0.01
Largest Tumor Dimension (cm)	1.00 (0.83–1.20)	1.00	0.93 (0.70–1.24)	0.62
Stage (%)				
I	ref.		ref.	
II	1.07 (0.13–8.79)	0.95	2.48 (0.22–28.1)	0.46
III	5.28 (1.82–15.4)	0.002	5.72 (1.34–24.5)	0.02
IV	9.09 (2.77–29.8)	< 0.001	4.04 (0.52–31.5)	0.18

[a] Floaters were defined as presence of free-floating tumor fragments noted within the fallopian tubes on final pathologic specimen analysis.
[b] Data as continuous decimal, ranging from 0 (no invasion) to 1 (100% invasion).

factors for progression, a wider set of patient characteristics was included in multivariate models, as the risk of death from any cause is impacted by the overall health of the patient. We considered comorbidities including hypertension, diabetes, major cardiovascular disease (congestive heart failure, myocardial infarction, or stroke), psychiatric disease, history of additional primary cancer, and smoking history.

Kaplan-Meier plots were constructed to visually compare time to progression and overall mortality with, and without the presence of floaters on final pathology, with and without adjustment. All analyses were performed using Stata 13.1 (Stata Corporation, College Station, TX).

3. Results

3.1. Included sample

Retrospective chart review was performed on 1022 consecutive patients diagnosed with uterine cancer presenting to our institution over a 6 year period from January 1st, 2005 to December 31st, 2010. The included cohort for this study was limited to a subset of 816 patients with Type 1 (n = 550) and Type 2 endometrial cancer (n = 266). Only four total patients were excluded for missing critical data. Within this sample, 20 patients (2.56%) were noted to have fragments of tumor cells noted within the fallopian tubes (floaters) on final pathology.

3.2. Baseline patient characteristics

Baseline patient characteristics for the cohort of patients, by

Table 4

Cox Proportional Hazard models for recurrence and death in a single institution cohort of patients with type I and type II endometrial adenocarcinoma, 2005–2010.

	Time to progression		Overall survival	
	Unadjusted HR (95% CI)	Adjusted HR[a] (95% CI)	Unadjusted HR (95% CI)	Adjusted HR[a] (95% CI)
Floaters[b]				
Not present	ref.	ref.	ref.	ref.
Present	3.22** (1.41–7.37)	1.10 (0.46–2.60)	1.84 (0.86–3.91)	0.57 (0.26–1.27)
Type I vs. II				
Type I	ref.	ref.	ref.	ref.
Type II	4.46** (2.95–6.75)	2.80** (1.78–4.42)	4.00** (2.97–5.40)	2.92** (2.05–4.15)
Stage				
Stage I	ref.	ref.	ref.	ref.
Stage II	1.86 (0.94–3.72)	1.78 (0.89–3.55)	1.98* (1.23–3.20)	1.57 (0.94–2.60)
Stage III	3.43** (2.09–5.63)	2.66** (1.58–4.49)	2.36** (1.59–3.51)	1.87* (1.21–2.88)
Stage IV	11.0** (6.22–19.52)	7.37** (3.99–13.6)	10.9** (7.30–16.1)	6.52** (4.05–10.5)
Age at diagnosis				
≤ 55 years	ref.	ref.	ref.	ref.
56–65 years			2.03** (1.20–3.45)	2.06* (1.14–3.73)
66–75 years	2.45** (1.37–4.40)	2.22** (1.23–4.00)	3.04** (1.80–5.14)	2.66** (1.46–4.87)
76–85 years			7.40** (4.32–12.7)	7.44** (3.99–13.9)
≥ 86 years			11.5** (5.78–23.0)	9.83** (4.19–23.0)
Race				
White	ref.	ref.	ref.	ref.
Non-white	1.86* (1.16–3.00)	1.62 (0.99–2.66)	1.48* (1.02–2.13)	1.46 (0.98–1.79)
Comorbidities				
Hypertension	–	–	1.71** (1.25–2.36)	1.37 (0.95–1.96)
Major CV disease[c]	–	–	3.71** (2.41–5.71)	1.84* (1.08–3.12)
Smoker (≥ 5 pack-years)	–	–	1.58** (1.15–2.19)	1.79** (1.25–2.56)
Other cancer	–	–	1.44 (0.94–2.22)	1.11 (0.69–1.79)

* $p < 0.05$.
** $p < 0.01$.
[a] Adjusted Hazard Ratios are adjusted for all other variables with estimates included in the given column of the table.
[b] Floaters were defined as presence of free-floating tumor fragments noted within the fallopian tubes on final pathologic specimen analysis.
[c] Includes congestive heart failure, myocardial infarction, and stroke.

presence or absence of floaters on final pathology are presented in Table 1. Patients with floaters were of similar age (65.6 vs 63.3 years, $p = 0.38$) and BMI (34.2 vs. 33.6; $p = 0.85$), and not significantly different in terms of parity, hormone use, or smoking status. Patients with floaters were significantly more likely to be diabetic (45.0% vs 23.8%; $p = 0.03$), however if the target alpha of 0.05 is adjusted for Bonferroni correction for multiple comparisons (15 characteristics considered), this p value does not meet the necessary threshold of 0.0033 for statistical significance. Overall, the small group of 20 patient's found to have floaters on final pathology mirrored the overall population characteristics of the cohort.

3.3. Description of cases with floaters

The 20 cases in which floaters were identified on final pathology are described in more detail, by Type I vs Type II, nuclear grade, pelvic washing status, and surgery type, in Table 2. Only 6 cases of floaters were identified among the 550 cases of Type 1 disease under review, 4 of which were found in patients with Stage I disease (stage IA n = 3; stage IB n = 1, implying that free floating fragments were found within the fallopian tubes without any coincident invasion of the adnexa. Despite these free floating fragments within the endometrial cavity, only 1 of the 6 (16.6%) cases with floaters in Type I disease also had positive pelvic washing cytology (stage IIIA due to presence of fallopian tube invasion).

Floaters were present in a significantly greater proportion of Type II disease specimens (5.3% vs 1.1%, $p < 0.001$), a total of 14 of 266 cases. Unlike in Type 1 disease, 71.4% of cases with floaters in Type 2 disease were in patients with Stage III or IV disease, and 42.9% of cases with floaters also had positive pelvic washing cytology. Among the 20

cases with floaters, 15 were nuclear grade 3, while 5 were nuclear grade 2, and no cases were nuclear grade 1. In the analysis of surgery type, a trend towards a higher rate of floaters in cases done laparoscopically or robotically (OR = 3.84; 95%CI 0.98-15.1), in which a uterine manipulator would have been placed.

3.4. Associations with surgical and pathologic characteristics

The cases included in this cohort were generally treated according to the standard of care in practice at the time. The majority of patients underwent surgery that included staging with pelvic lymph node dissection (89.0%) and paraaortic lymph node dissection (71.2%), and, less commonly, additional procedures such as omentectomy (26.9%) or appendectomy (3.5%). The majority of patients underwent adjuvant treatment with vaginal brachytherapy (71.7%), while adjuvant carboplatin and paclitaxel chemotherapy was more commonly used for Type II cancers (65.1%) than Type I cancers (17.2%). Most patients that did not undergo adjuvant treatment had Type I disease (89.1%) with < 50% invasion (94.2%).

Associations of the presence of floaters with surgical approach and other pathologic characteristics from the final specimen are presented in Table 3. In unadjusted bivariate logistic regression, the presence of floaters was positively associated with Type II disease, nuclear grade 3 (vs. grade 1 or 2), presence of lymphovascular invasion, and overall stage III or IV. As floaters were more common in Type II disease, and Type II disease is known to be associated with more extensive disease, it was necessary to use multivariate logistic regression to more accurately explore these associations.

In adjusted analysis, the type of disease was found to be unrelated to the presence of floaters (OR = 1.77; 95%CI 0.21-14.6). The association

(A)

(B)
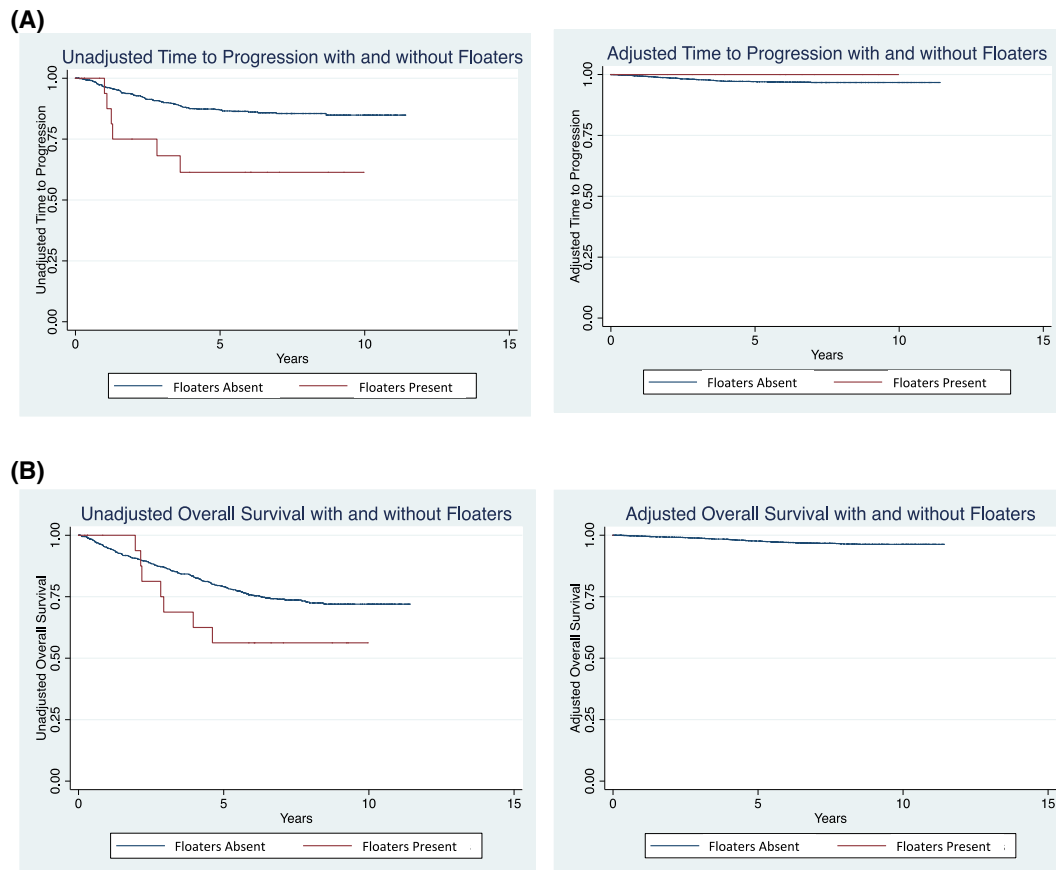
[1] Note that for Adjusted Overall Survival in the right panel of (B), the two survival curves are essentially identical, and therefore overlaid and may appear as a single curve.

Fig. 1. Kaplan-Meier Survival Plots, adjusted and unadjusted, for (A) Time to Progression and (B) Overall Survival[1], by presence or absence of free floating tumor fragments within the fallopian tubes ('floaters'), in Type I and Type II endometrial cancer, single institution cohort presenting 2005–2010.

of floaters with higher nuclear grade was similarly eliminated with adjustment. However, with multivariate adjustment, significant associations of floaters with positive lymphovascular invasion (OR = 9.65; 95%CI 2.35-39.6) and Stage III disease remained. Additionally, the extent of myometrial invasion was inversely related to the likelihood of observing floaters, with an OR of 0.08 for comparing no invasion to 100% invasion. Furthermore, a trend was observed towards an association of floaters with laparoscopic/robotic approach and uterine manipulator use (OR = 3.84; 95%CI 0.98-15.1; $p = 0.054$).

3.5. Analysis of time to progression

In unadjusted analysis, floaters were significantly associated with risk of progression/recurrence of disease (HR = 3.22, 95%CI 1.41-7.37), however this association was eliminated with adjustment for risk factors (HR = 1.10, 95%CI 0.46-2.60, Table 4). In addition to cancer type (Type 2 vs Type 1) and stage (Stage III and IV vs Stage I), patient characteristics associated with increased risk of recurrence in adjusted models included age > 65 (HR = 2.22, 95%CI 1.23–4.00) and a trend towards increased risk in nonwhite race (HR = 1.62; 95%CI 0.99–2.66). As there is no biologic basis for patient medical co-morbidities to impact disease recurrence, these variables were not found to be significantly associated with the outcome at hand, and were excluded from adjusted models for time to progression. Complete Cox regression data and Kaplan-Meier survival plots for unadjusted and adjusted analyses of time to progression can be seen in Table 4 and Fig. 1, respectively.

3.6. Analysis of overall survival

Floaters were not associated with decreased overall survival in unadjusted (HR = 1.84, 95%CI 0.86-3.91) or adjusted (HR = 0.57, 95%CI 0.26-1.27) analysis. In the adjusted model, patients with Type 2 disease were at significantly increased risk of death (HR = 2.92, 95%CI 2.05-4.15). Increasing disease stage and patient age were also tightly associated with risk of death. History of smoking and of major cardiovascular disease (congestive heart failure, myocardial infarction, or stroke) at the time of diagnosis were significantly associated with risk of death (HR = 1.79, $p = 0.001$; HR = 1.84, $p = 0.025$, respectively). Interestingly, non-white race remained a near significant predictor of increased risk of death, even in the adjusted model (HR = 1.46; 95%CI 0.98–2.18; $p = 0.066$). Complete Cox regression data and Kaplan-Meier survival plots for unadjusted and adjusted analyses of overall survival can be seen in Table 4 and Fig. 1, respectively.

4. Discussion

The true incidence and etiology of floaters is unknown and there is scant evidence about their relationship with recurrence and survival. Furthermore, the presence of floaters does not play a role in the FIGO Staging System for endometrial cancer (Pecorelli et al., 2009). Therefore, when this pathologic finding is encountered, there exists a diagnostic and therapeutic conundrum: In early stage cancers with floaters, should patients be treated similar to a Stage IIIA with adnexal involvement or should they be treated as a Stage I with floaters being a non-significant incidental finding?

We report an overall incidence of floaters of 2.5%, which is within range of the only published incidence rate. Delair et al. reported a range from 2 to 11%; 2% when laparoscopic hysterectomy was performed and 11% when Robotic-assisted laparoscopic hysterectomy was performed (Delair et al., 2013). Our data showed that floaters were more common in Type II disease specimens when compared to Type I specimens (5.3% vs 1.1%, $p < 0.001$). In addition, it was found that in early stage disease, floaters were more common in Type II cancers (2.45% vs 0.83%; $p = 0.107$). When looking at both risk of recurrence and death, however, the presence of floaters did not appear to play a significant or causative role. Thus, it is more likely that in Type II cancer, where stage at presentation was often more advanced, it is the extent of disease and overall aggressiveness which are responsible for the high risk of recurrence and death, and likely not the presence of floaters within the fallopian tube lumen.

Given that positive washings in the setting of floaters is three times more likely in Type II versus Type I cancers, it could further be assumed that it is the late stage of presentation in Type II cases which causes positive washings versus the floaters themselves. Based on these results, there should be no change in management practices based on the presence of floaters in Type II cancers.

In early stage disease, there was no increased risk of recurrence or death when floaters were present. It stands to reason that the presence of floaters is somewhat analogous to the presence of positive peritoneal cytology, in that it is a pathologic finding without major prognostic impact in the setting of otherwise, low risk disease (Zaino, 2009). Therefore, based on the current available data, for both Type I and Type II cancers, we do not recommend the presence of floaters be considered as a factor in determining whether or not a patient needs adjuvant therapy.

We also find evidence that, controlling for cancer stage and other pathologic findings, floaters were more likely to be found in cases performed laparoscopically or robotically as compared to abdominal hysterectomy (HR = 3.85, $p = 0.05$ for all stages, HR = 7.34; $p = 0.05$ for stage I or II). This finding indicates the possibility that floaters could sometimes be a result of tissue dislodged by intra-operative use of a uterine manipulator, a theory that was also proposed by Delair et al.[11] Uterine manipulators have been previously postulated to cause higher rates of positive peritoneal cytology and "psuedo" lymphovascular space invasion by disruption of tissue (Sonoda et al., 2001; Logani et al., 2008). However, both of these associations, as well as any impact on outcomes from uterine manipulator use have been discounted in a number of more recent studies (Hopkins et al., 2014; Lee et al., 2013; Momeni et al., 2013; Rakowski et al., 2012; Zhang et al., 2014).

The major limitation to this study is that it was retrospective in nature and limited to a single institution. As this study was conducted retrospectively, no prospective power analysis was performed for the question at hand. We recognize that the small number of cases limited our power to detect a small difference in rare outcomes, in particular for death and thereby overall survival. With that being said, there is a scarcity of data on the role of floaters as a pathologic finding, their association with other pathologic findings, and their impact on patient outcomes. Our findings are the first of their kind and further pooled data would be useful.

Conflict of interest statement

The authors of this manuscript have no conflicts of interest to disclose.

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